AN EXPERIMENTAL STUDY OF THE THYROID GLAND OF DOGS, WITH ESPECIAL CONSIDERATION OF HYPERTROPHY OF THIS GLAND

BY

WILLIAM S. HALSTED, M. D.

Professor of Surgery in the Johns Hopkins University and Surgeon-in-Chief to the Johns Hopkins Hospital

---

(REPRINTED FROM JOHNS HOPKINS HOSPITAL REPORTS, VOL. I.)

BALTIMORE
THE JOHNS HOPKINS PRESS
1896

AN EXPERIMENTAL STUDY OF THE THYROID GLAND OF DOGS, WITH ESPECIAL CONSIDERATION OF HYPERTROPHY OF THIS GLAND.

BY

WILLIAM S. HALSTED, M. D.

[*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*]

(REPRINTED FROM JOHNS HOPKINS HOSPITAL REPORTS, VOL. I.)

BALTIMORE
THE JOHNS HOPKINS PRESS
1896

AN EXPERIMENTAL STUDY OF THE THYROID GLAND OF DOGS, WITH ESPECIAL CONSIDERATION OF HYPERTROPHY OF THIS GLAND.

By WILLIAM S. HALSTED, M. D.

[From the Pathological Laboratory of the Johns Hopkins University and Hospital.]

In 1887 Munk* made the remarkable statement that dogs survived experiments which deprived them of the function of the thyroid gland (Ausschalteversuche), provided that the wounds healed "well" by first intention; but if swelling of the wound supervened, swelling of an inflammatory or œdematous nature, swelling dependent upon hemorrhage or upon an accumulation of the secretions of the wound, then very soon appeared the symptoms characteristic of extirpation of the thyroid gland. These symptoms, developing possibly somewhat slower than after extirpation of the gland, became gradually more and more pronounced and finally the animal succumbed. In some cases, those in which the swelling subsided in a short time, the symptoms disappeared and the dog made a perfect recovery. If there was an accumulation of pus in the depths of the wound, or if there was suppuration enough to be perceptible, the dogs, without exception, died as promptly as if complete extirpation had been performed.

Munk performed his operation for complete isolation of the thyroid gland as follows: after doubly ligating and dividing the veins which leave the lower ends of the thyroid lobes and, when necessary, doubly ligating and dividing the vessels which go to and from the sides of the glands, he lifted them out of their so-called capsules and completely severed their active connection with the body of the animal by ligation of the vessels and nerves of the hilus. He then returned the lobes to their original position, and in

*Hermann Munk: Untersuchungen über die Schilddrüse. Sitzungsberichte der königlich-preussischen Academie der Wissenschaften zu Berlin, 1887.

order to keep them the more perfectly in place he tied together the ligatures which had been applied to their lower veins.

Nine dogs survived Munk's isolation experiments. He does not give the number of his experiments. At Munk's instigation, Boginsky repeated these experiments and reported identical results.

Particularly surprising was the statement that "whenever a considerable portion of the lobes became attached the symptoms of thyroid extirpation manifested themselves, and the dogs with few exceptions died; whereas the other dogs whose lobes had either entirely disappeared or had in exceedingly small parts become attached, remained free from all symptoms and continued to live in the enjoyment of good health."

Whenever the wounds healed well by first intention the thyroid gland had in eight or ten days entirely or almost entirely disappeared. When there was a transitory swelling of the wound and when, nevertheless, the dogs recovered from the experiment, he found even after from two to five months that the thyroid lobes had become attached and were of considerable size. Munk reserved for a subsequent communication* his explanation of these results. He compelled one, nevertheless, to anticipate that he proposed to regard the thyroid gland as a superfluous organ and to attribute the fatal results which attend extirpation of the thyroid gland to injuries done to nerves. That the injury to the nerves should necessarily be less from the operation for isolation than from the operation for extirpation of the thyroid glands I could not conceive.

Of the several unsatisfactory interpretations of the results of Munk's experiments which suggested themselves to me was one which promised for these experiments an important practical bearing upon surgery, and induced me soon after the appearance of Munk's paper to repeat them. Although Munk believed his experiments to be a refutation of Schiff's transplantation experiments I thought that I saw in them a possible confirmation of Schiff's work.

Munk could not find in dogs the accessory thyroid glands which are probably invariably and certainly almost invariably present, and might, I thought, have failed to see the attached remains of an

*Sitzungsberichte der königlich-preussischen Academie der Wissenschaften zu Berlin, 1888. Munk speaks here of lesions of the laryngeal and vago-sympathetic nerves.

isolated thyroid lobe, or to observe that a little active thyroid tissue remained in the otherwise necrotic gland. His isolation experiments were practically transplantation experiments; and I was encouraged from my interpretation of his results to believe that it might be possible to transplant a thyroid lobe from one dog to another, and a part of the thyroid gland from man to man.

To repeat Munk's work was to make three experiments in one. For whatever might be the effects produced by isolation of the thyroid lobes the experiments would at least be equivalent to transplantation experiments under most favorable conditions, and should the glands become necrotic and fail to be reinstated as glandular organs the isolation experiments would be equivalent also to extirpation experiments.

EXAMPLES OF COMPLETE ISOLATION OF BOTH THYROID LOBES.

EXAMPLE 1. *Isolation of both Thyroid Lobes by Ligation. Munk's Operation.* Dog 23. February 28, 1888.

The wound was closed with buried skin sutures of silk and dressed with horse-hair. The dressing was held in place by a plaster of Paris bandage.

March 2. The dog has trismus. Tonic spasms of his legs developed while his temperature was being taken. These spasms subsided completely before the thermometer was removed. Tem. 39°. Resp. 33.

March 3. The dog has conjunctivitis of both eyes. It is more pronounced in the left than in the right eye.

March 4. The right eye is clear. The conjunctivitis in the left eye is worse. Temp. 39°. Resp. 19. There is a persistent erection of the penis. There are fibrillary tremors of the tongue and of the muscles in general. Temp. 38.5°. Resp. 18 and labored.

March 9. The dog drinks milk freely, but is very weak. His tremors are less marked.

March 12. The dog is found dead.

Autopsy. The wound is beautifully healed, the cicatrix scarcely visible. The thyroid lobes are firmly adherent to the surrounding tissues. There is a greyish yellow semi-fluid zone beneath the capsules of the thyroid lobes. The left lobe is completely surrounded by this zone, which is about 2 mm. thick. The right lobe is sur-

rounded only at its lower end by this zone. The upper two-thirds of the right lobe is of a mottled color. All the organs appear to be healthy.

Microscopical Examination of the Fluid Subscapular Zone. The fluid contains no pus, but is rich in large cells which are filled with fat molecules. These cells have about the size of large leucocytes.

Microscopical Examination of the Upper Part of the Right Thyroid Lobe. There is an exquisite fatty degeneration of the periphery of the lobe. This zone of degeneration is about 3 mm. deep. In the central portion of the lobe the gland structure can be made out. The follicles seem to be lined and sometimes partly filled with epithelium. The epithelial cells contain no fat, and the nuclei either do not stain at all or stain very feebly with Bismark brown. The cells have a homogeneous, glistening appearance. There are many colorless acicular crystals (fat crystals) among the epithelial cells. Yellow amorphous and crystalline hæmatodin is scattered through the central portion of the lobe and also in the peripheral fatty zone. In the peripheral zone the outlines of the follicles are almost lost. Leucocytes have wandered in from the capsule of the lobe along the connective tissue septa between the follicles.

EXAMPLE 2. *Isolation of both Thyroid Lobes by Ligation.* Dog 24.. February 28, 1888.

The wound was closed with buried sutures and dressed with horse-hair. The dressing was held in place by a plaster of Paris bandage.

March 1. The dog takes milk eagerly and without immediate bad effects.

March 4. Soft yellow stools. Temperature 39°.

March 5. The dog has fibrillary tongue spasms.

March 8. The fibrillary spasms continue.

March 9. The dog has no tongue spasms.

March 13. There are fibrillary contractions at the tip of the dog's tongue, but no other spasms. The dog drinks milk freely.

March 14. The dog is found dead.

Autopsy. The wound is beautifully healed. The tip and edges of the tongue have sloughed away. Both thyroid lobes are firm and very large and adherent to the surrounding tissues.

Microscopical Examination of Frozen Sections. Organization of the glands is going on from the periphery towards the centre. The leucocytes have wandered in along the septa of the glands, and new tissue is forming in place of the old which is necrotic.

The thyroid lobes of twenty-four dogs were isolated in the way which Munk describes. The wounds of twelve of these healed absolutely per primam.* All of the dogs died in from two to nineteen days, and with the symptoms which are characteristic of extirpation of both lobes. The isolated lobes of the dogs whose wounds healed per primam were without exception necrosed. Absorption of the lobes began almost immediately, and in some instances had progressed so far that no trace of them remained except a yellowish stain of the tissue in which they had been imbedded (vid. Table II). One dog (No. 59) remained perfectly well for sixty days after the isolation of both lobes and until killed by other dogs. His neck was so mangled by the teeth of the dogs that it was impossible to find the accessory thyroid glands or any trace of the isolated lobes. I regard this as one of the very few but undoubted instances of survival of dogs after extirpation of both thyroid lobes. We consider it a very great misfortune that this dog, which interested us perhaps more than all of the others, should have been killed, and furthermore, so mangled that we could learn nothing from the autopsy. The constant or almost constant presence of accessory thyroids explains the fact that dogs occasionally survive the extirpation of both lobes. Our piecemeal extirpation experiments have proved that some dogs may live with the one-eighteenth part or less of both lobes. But we have occasionally found the sum of the accessory thyroids to be apparently greater than this and still insufficient for the life of the dog.

The quality of the gland and the individual requirements of the animal are factors about which we know little, and which may be more important than the actual quantity of thyroid tissue.

* The wounds of eight dogs suppurated. Two dogs died on the second day or too early to permit one to say positively that the wounds had healed per primam; and in two instances the wounds were found distended with blood at the autopsy. If it had occurred to me at the outset to use the buried skin sutures I believe that fewer cases would have suppurated; for of the five cases which antedated the use of buried skin sutures, four suppurated, and of the nineteen cases in which these sutures were used only four suppurated.

We have made sixty-three total extirpations of the thyroid lobes.* All of the dogs except the one referred to (No. 59) died in from two days to three weeks, and almost invariably with the typical symptoms (vid. Table III). Of eighty-eight transplantations† of the thyroid lobe into the neck not one was successful. In fifty-three of these the wound healed per primam. In two or three instances small vessels had invaded the periphery of the necrotic gland and had converted a thin zone of the cortex into connective tissue. In the genuine transplantation experiments the transplanted lobes were absorbed just as promptly as the isolated lobes in Munk's experiments (vid. Tables II and IV).

PARTIAL ISOLATION OF BOTH THYROID LOBES. THE LARGE BRANCH OF THE THYROID ARTERY WHICH GOES TO THE UPPER POLE AND THE VEIN FROM THE LOWER POLE ARE NOT LIGATED; OTHERWISE BOTH THYROID LOBES ARE COMPLETELY ISOLATED.

EXAMPLE 1. Dog 104. April 19, 1889. Open wound.

April 28. The dog seems perfectly well. The wound is healed.

April 30. The dog has tongue tremors and makes the licking movements with the tongue which we have frequently observed in dogs whose thyroids have been extirpated.

May 1. The tongue tremors are less pronounced. The licking movements are still vigorous.

May 7. The tongue tremors are pronounced. The dog has no general spasms.

May 14. The tongue tremors are very faint.

May 28. Dog seems perfectly well.

June 24. Hair is falling out, particularly over the eyes.

June 25. The dog has escaped.

June 27. Returned of his own accord. The hair is very thin all over his body. He scratches himself constantly. The œdema

*Thirty-seven of these are recorded as such. Twenty-six piecemeal experiments are not so recorded, for they are of interest chiefly in this, that they were made to determine approximately the time of the first indications of hypertrophy in one lobe after excision of the other.

†Munk's isolation experiments, as already explained, are equivalent to transplantations, and have been counted as such.

caused by the scratching gives to the skin about the face and head somewhat the appearance of myxœdema.

July 10. Has lost most of his hair. He is very anæmic. His blood is used for direct transfusion into dog 109.

Autopsy. Both thyroid lobes are large and hard and very firmly bound down to the surrounding tissues by adhesions. With the microscope they were found to be hypertrophied. I believe, judging from the next example (dog 103), that this dog would have died ultimately with the symptoms of thyroid extirpation.

EXAMPLE 2. Dog 103. April 19, 1889. The wound is left open. The dog was profoundly depressed after the operation.

April 27. There is conjunctivitis of both eyes. The wound is doing well.

April 28. The dog has symptoms which are characteristic of extirpation of both thyroid lobes. He shivers, has tongue tremors and general tonico-clonic spasms. His gums are inflamed. The membranæ nictitantes are conspicuous. He groans with each expiration.

April 30. The tongue tremors persist. The general spasms have ceased. The conjunctivitis is more pronounced. There is a very offensive gingivitis. Dog makes peculiar, almost incessant licking movements with his tongue. These peculiar licking movements have been frequently observed by me in dogs whose thyroid glands have been extirpated.

May 1. Seems better. He still has tongue tremors.

May 3. His hind legs are slightly stiff. The tongue tremors are scarcely perceptible.

May 7. The tongue tremors are a little more distinct. The conjunctivitis has almost subsided.

May 14. The tongue tremors are very faint. There is no conjunctivitis.

May 19. All the symptoms of extirpation of both thyroid lobes have reappeared.

May 21. The dog seems much better. The tongue tremors are very faint. There are no other symptoms. There is a slight subconjunctival injection.

May 23. Except for the faint tongue tremors the dog seems fairly well. He eats well, but is very thin.

May 24. Has no tongue tremors, but strong clonic spasms of the

flexor muscles of all of his legs. The spasms of the temporal and ear muscles are especially pronounced.

May 25. Dog has no spasms and is much better.

June 14. All the symptoms of double extirpation have re-appeared.

June 15, A. M. Is found dead.

Autopsy. The left thyroid weighs 3 grms. and is very hard. The right thyroid weighs 1 grm. For the microscopic appearance of both lobes see Plate X, Fig. 7. The fatal result in this and the preceding case (104) is to be attributed probably to extensive destruction of the glands by blood extravasation. Otherwise we could not regard the changes which we designate as hypertrophy as very highly compensatory; for, notwithstanding the fact that the glands weighed two or three times as much as normal and showed the most advanced stage of hypertrophy, one dog died with symptoms of total extirpation and the other had the symptoms which I have described (dog 104), and would probably have died of thyroid privation.

Piecemeal Extirpation of the Thyroid Gland.

Example 1. Dog 81. *Operation* 1. Oct. 4, 1888. *Removed the lower half of the left thyroid lobe.* The piece removed weighs 0.45 grm. and is normal. The wound was left open and without a dressing.

Oct. 13. The dog seems quite well. His gums are abnormally pale. There are no symptoms of thyroid extirpation.

Nov. 22. Has been quite well since the operation.

Operation 2. Nov. 23. Fifty days after the first operation. *Removed the upper, the remaining half of the left thyroid and the lower third of the right thyroid lobe.* The wound was left open and without a dressing. The upper half of the left thyroid weighs 0.70 grm. The right gland is large and would weigh about 2 grms.

Nov. 24. Seems perfectly well.

Dec. 5. The dog has apparently been well ever since the last operation. The membranæ nictitantes seem to be abnormally conspicuous.

Jan. 10, 1889. Three or four days ago began to cough. He is less lively than heretofore, and has a slight conjunctivitis. He eats well.

Feb. 1. Acts as if he were partially blind and abnormally stupid. He does not see meat which is thrown to him; he finds it by the sense of smell. Dr. Randolph has to-day examined the dog's eyes ophthalmoscopically and pronounces them normal.

April 30. Is stupid and partially blind; otherwise apparently well.

Operation 3. April 30. *Removed the lower half of what remained of the right thyroid—its middle third.* The piece removed weighs 1 grm.

August 9. The dog is well, but is slow to see and catch his food.

Operation 4. August 9. *Removed the second sixth of the right thyroid gland—the lower half of the remaining third.* There remains to the dog one-sixth of one thyroid lobe.

August 24. Has been well since the last operation. This A. M. he was strangled to death by the impaction of a large piece of meat in his œsophagus.

Autopsy. The dog is very well nourished. The wound is healed. There are two accessory thyroids under the arch of the aorta, and one at the lower border of the hyoid bone on the thyro-hyoid membrane. All the organs are apparently healthy. The aortic thyroids show a more advanced stage of hypertrophy than does the gland which was found on the thyro-hyoid membrane. Usually the accessory thyroids and the remainder of the thyroid lobes are hypertrophied to a like degree.

Piecemeal Extirpation of the Thyroid Gland.

Example 2. Dog 86. *Operation* 1. Oct. 23, 1888. *Excised the lower half of the left thyroid lobe.* The wound is left open and without a dressing. The piece weighs 0.6 grm. Its structure is normal.

Dec. 12. Dog has been perfectly well since the first operation.

Operation 2. Dec. 12. *Excised the upper half of the left and the lower half of the right thyroid lobe.* The wound was left open and without a dressing. The upper half of the left thyroid lobe weighs 2 grms., and the lower half of the right 1 grm. The left lobe was slightly adherent to the surrounding parts. For the structure of

the pieces removed see Plate X, Figs. 5 and 8, and Plate IX, Fig. 8.

Feb. 12, 1889. Dog has been perfectly well since the last operation.

Operation 3. Feb. 12. *Excised one-half of the remaining upper half of the right lobe (its second fourth).* The wound is left open. The excised piece is typically hypertrophied (vid. Plate X, Fig. 8).

April 27. Dog has been perfectly well since the last operation.

Operation 4. April 28. *Excised the lower half of the remaining upper fourth of the right lobe—the second eighth of the right thyroid* (vid. Plate X, Figs. 6 and 7).

There now remains to the dog one-eighth of one thyroid lobe, or one-sixteenth of the gland.

May 19, A. M. Is found dead. Has had all the symptoms of double thyroid extirpation for about two weeks, and has refused food since May 2.

Autopsy. The wound is healthy and nearly healed. Over the thyro-hyoid ligament in the median line, and partially concealed behind the hyoid bone, is an accessory thyroid about the size of a very small bean. The remaining eighth of the right lobe weighs about 0.8 grm.

There is a small bean-like accessory thyroid gland under the skin about one inch above the sternum; also a chain of four enlarged aortic thyroids. The accessory thyroids have the structure which we call hypertrophy. The hypophysis cerebri has the size of a large French pea. All the organs appear to be healthy.

Piecemeal Extirpation of the Thyroid Gland.

Example 3. Dog 90. *Operation* 1. Oct. 1888. *Excised the lower half of the left thyroid lobe.* The wound is left open and without a dressing. The piece removed weighs 0.3 grm. Its structure is normal.

Nov. 20. The dog has been fairly well since the operation, but his hair is falling out. He is entirely bald about the right eye.

Dec. 30. Has a cough and been quite sick for three or four weeks. Has probably had pneumonia and is now convalescing.

Jan. 29, 1889. The dog has been well since Jan. 1.

Operation 2. *Removed the upper half of the left and the lower two-fifths of the right thyroid lobe.*

Both lobes seem to be hypertrophied, and both are adherent to the surrounding tissues. The left one is very firmly bound down by adhesions. For the stage of hypertrophy of the pieces removed see Plate X, Fig. 8, and Photo. V.

April 30. The dog has been perfectly well since the last operation. He is sire to the pups with the enormously hypertrophied thyroids thrown by bitch 97 on the 13th of April.

Operation 3. April 30. *Removed the lower half of the remaining three-fifths of the right thyroid lobe.* The piece removed weighs 1.5 grm. For the minute structure see Plate X, Fig. 8, and Photo. V.

June 20. Since the last operation the dog has been growing sluggish and stupid. When released from his cage he takes a few steps and then lies down. He has had no convulsions nor tremors.

June 21. Died this morning.

Autopsy. The remaining portion, the upper three-tenths of the right thyroid lobe, weighs 2 grms. For the structure see Plate X, Figs. 5 and 8, and Photo. V. It is very firm and has a nearly globular shape. Accessory thyroid glands were not found at the autopsy which, however, was made in my absence. There is general pulmonary œdema. The other organs appear to be healthy. The dog was not emaciated. There is no apparent œdema of the subcutaneous tissues.

Piecemeal Extirpation of both Thyroid Glands.

Example 4. Dog 97. *Operation* 1. Nov. 14, 1888. *Removed the upper third of the left lobe.*

The piece removed has a normal structure. The wound was left open.

Dec. 12. The dog (bitch) has been perfectly well since the operation.

Operation 2. *The neck was opened through the cicatrix for the purpose of removing what remained of the left thyroid.*

The ligature which had been applied at the first operation was found imbedded in a little new tissue. Not a trace remained of the left thyroid.

April 11, 1889. The bitch is at full term. Has convulsions and behaves precisely as do the dogs whose thyroids have been completely extirpated.

April 12. Had to-day three or four convulsive seizures. Each attack lasted about one hour. Otherwise the bitch seems well and in good spirits.

April 13. Bitch has whelped five pups. Two alive and three dead. Dog 90 is sire of the pups. He impregnated this bitch when he had been deprived of all of one lobe and two-fifths of the other, and when she possessed only one lobe. The pups which were born alive died this evening. The thyroid glands of these pups are many times (at least 20 times) larger than normal. See Plate X, Fig. 9, *c*. Compare with normal thyroid of new-born pup, Fig. 9, *a*, and photographs.

Operation 3. April 30. *Removed the lower half of the right thyroid gland.* The gland is very large and decidedly spindle-shaped. It is hypertrophied. See Plate X, Fig. 7.

Nov. 11. Has been well since the last operation.

Operation 4. Nov. 11. *Removed what I believed to be the second fourth—the lower half of the remaining half—of the right thyroid lobe.*

Jan. 1, 1890. The piece removed Nov. 11th was to-day examined and supposed to be lymphatic gland tissue. Unfortunately the specimen of this piece has been lost.

I now suspect that it was thyroid gland and not lymphatic* tissue.

Operation 5. Jan. 6. *Explored the right side of the dog's neck very carefully. Could find nothing but a small nodule, at the lower end of which was what seemed to be a ligature of the previous operation. Removed this nodule.* It proved to be hypertrophied thyroid tissue. Vid. Plate X, Fig. 7.

Jan. 13. The dog has tongue tremors and general spasms and behaves as do the dogs whose thyroids have been extirpated.

Jan. 14. Is dead.

Autopsy. Nothing remains of either thyroid lobe. An unusual number of hypertrophied accessory thyroids are found; viz., one in front of the arch of the aorta; three behind the arch near the origin of the ductus Botali; one large gland, 3 mm. × 4 mm., behind the ster-

* We have twice labeled as *lymphatic tissue* specimens which we subsequently found to be thyroid tissue in the extreme stage of hypertrophy.

num. For the minute structure of these hypertrophied glands vid. Plate X, Fig. 7. This figure is intended to represent the most advanced stage of hypertrophy; but it is very badly executed.

Piecemeal Extirpation of the Thyroid Gland.

Example 5. Dog 126. *Operation* 1. Dec. 1888. *The lower end of the left thyroid gland was ligated at about* 2 *mm. above its tip.* The wound is left open.

April 22, 1889. The dog has been perfectly well since the operation.

Operation 2. One hundred and thirty-two days after the first operation. *Removed the remainder of the left and the lower two-fifths of the right thyroid gland.* Both glands were hypertrophied. Vid. Plate X, Figs. 6 and 7, and photograph. There were no adhesions binding the thyroids to the surrounding tissues. The tied-off tip of the left lobe is converted into connective tissue. Here and there traces of follicles remain in this tip.*

Aug. 9. Dog has been perfectly well since the last operation.

Operation 3. *Removed the lower half of the remaining three-fifths of the right thyroid gland.*

For the minute structure vid. Plate X, Figs. 6 and 7.

Nov. 11. Dog has been very weak since the third operation and was scarcely able to walk when he was put on the table to be anæsthetized.

Autopsy. What remains of the right thyroid gland weighs 0.75 grm. and is hypertrophied. Four accessory thyroids were found, two below and one behind the arch of the aorta, and one behind the hyoid bone at the upper end of the thyro-hyoid membrane. The accessory thyroids were all hypertrophied, although very small. Not one of them was larger than a grape-seed. The dog has no myxœdema. For the minute structure of the hypertrophied accessory thyroids vid. Plate X, Figs. 5 and 8, and Photo. V.

Piecemeal Extirpation of the Thyroid Gland.

Example 6. Dog 127. *Operation* 1. Dec. 11, 1888. *Ligated the lower end of the left thyroid gland at about* 3 *mm. from its tip.* The piece ligated was not cut off. The wound is left open.

* In dog 127 the tied-off tip retained its original structure, and the operation (ligation of tip) was not followed by hypertrophy. See Example 6.

April 22, 1889. The dog has been perfectly well since the operation.

Operation 2. *Removed the remainder of the left thyroid and the lower third of the right thyroid gland.* The wound was left open. The pieces removed were, much to my surprise,* normal 132 days after ligation of the inferior tip of the left lobe.

August 30. About nine weeks ago the bitch was impregnated by a good-sized, healthy, unoperated dog.

She is about at full term and has to-day developed the symptoms characteristic of extirpation of both thyroid glands. She has tongue tremors and general clonico-tonic spasms.

Sept. 1. Last night she gave birth to eight dead pups and seems perfectly well this morning. The thyroids of these pups are at least twelve times as large as normal.

Nov. 11. The dog has been well since the last note.

This is the second opportunity that we have had to observe the effect of pregnancy upon a bitch deprived in part of the thyroid gland. In both cases for a few hours, less than twenty-four, just prior to whelping the symptoms of complete thyroid privation manifested themselves although each animal still possessed much more than enough thyroid gland for her ordinary wants.

It is interesting to note that pregnancy has already been supposed to have an influence in producing tetany, and that in at least two or three instances† it has been suspected that the tetany was caused by the complete or partial absence of the thyroid gland.

Operation 3. *Removed the lower half of the remaining two-thirds of the right thyroid gland.* The gland is large, hard and very vascular, and shows, microscopically, an early stage of hypertrophy.

*I say *much to my surprise*, because in the preceding case (dog 126) the same operation was followed by hypertrophy in the same number (132) of days. But longitudinal sections of the entire lobes revealed the cause of the hypertrophy in the one case and the reason for its absence in the other. In both cases fragments of the ligature were found imbedded in a narrow connective tissue zone two or three millimeters above the inferior pole; but in 127 the gland tissue below the ligature was intact or very slightly modified by a little increase in connective tissue, whereas in 126 only an occasional trace of the gland remained.

† Thomas, H. M. Tetany in Pregnancy, Johns Hopkins Hospital Bulletin, May 20, 1895.

Jan. 14, 1890. The dog has been perfectly well since the last operation and has grown very fat.

Operation 4. *Removed the lower two-thirds of the remaining upper third—the second and third ninths—of the right thyroid gland.*

The piece removed weighs 1.5 grms. It shows, microscopically, an advanced stage of hypertrophy. The gland was very adherent to the tissues surrounding it.

The dog is now reduced to one-eighteenth of both thyroids. The piece remaining—the upper ninth of the right thyroid—would probably weigh as much as the entire right thyroid originally weighed. The dog has been getting steadily fatter since the first operation, and now is enormously fat and well. There are no evidences of myxœdema. The dog seems mentally as active as ever.

Operation 5. Jan. 1891. Removed the superior ninth, the remainder of the right thyroid gland.

The dog died within three days of the last operation.

Autopsy. A chain of accessory thyroids was found behind the arch of the aorta, and one accessory thyroid on the thyro-hyoid membrane, behind the hyoid bone.

These glands were not as large as I have several times found them. They were preserved, but cannot be found. What I have said about them is from memory.

The piecemeal resection experiments demonstrated conclusively that the symptoms which manifest themselves after extirpation of both thyroid lobes are due to the loss of thyroid tissue, and not to the injury to the nerves of the neck, as Munk and others have supposed.

What part of both lobes a dog requires we have not tried to determine. It is probably never precisely the same for two dogs, and may depend somewhat upon the time allowed to intervene between the operations. Very few dogs can live with the accessory thyroids alone.

Dog 81 survived the excision in four operations of eleven-twelfths of the two thyroid lobes. He was in good condition when he died of strangulation from swallowing too large a piece of meat. Three small accessory thyroids were found at the autopsy.

Dog 86 enjoyed good health with one-eighth of the two lobes; but he died twenty-one days after the fourth operation, at which he was

reduced to one-sixteenth of the two lobes. The fourth operation was performed six months after the first operation. For two weeks before his death he had the symptoms characteristic of total excision. At the autopsy five accessory glands were found, and the remaining piece of the hypertrophied right lobe weighed nearly one grm.

Dog 90 was reduced to about one-tenth of both lobes in six months by three operations. He died three weeks after the third operation, without active symptoms. The superior fifth or perhaps three-tenths of the right thyroid which was excised at the autopsy weighed one and one-fifth grammes.

Dog 97 when deprived of only one lobe developed the typical total extirpation symptoms a few hours before her pups were born. Nevertheless she recovered completely from the two subsequent operations and did not die until the final fragment of the right lobe was removed at the fifth operation. She died one week after the last operation—fourteen months after the first operation, and when nothing remained to her of the two thyroid lobes. An unusual number of accessory thyroids were found at the autopsy. What proportional part of both lobes the final piece represented I cannot say.

Dog 126 lived only three months with about one-tenth of the two lobes and with at least four accessory thyroid glands. The four operations were performed in eleven months.

Dog 127 enjoyed good health with one-eighteenth of the two lobes. This eighteenth weighed almost as much as the two lobes normally weigh. He died after the fifth operation, two years after the first operation, and not until the final piece had been excised. The accessory thyroids were not as large as we had expected them to be, nor as large as we have several times found them.

One of the most interesting discoveries to which our experiments led was the hypertrophy of the thyroid glands of the new-born pups of dogs whose thyroid lobes had been in part excised. The glands of all five of the pups of bitch 97 were about twenty times as large as normal. See Plate X, Fig. 9, *a* and *c*, and Photograph 10. In all of the pups the two lobes seemed to be connected by a deep isthmus. Vid. Plate X, Fig. 9, *c*, and Photograph 10. The lobes and isthmus together made a horse-shoe-shaped gland which embraced and almost surrounded the trachea. Our efforts to con-

firm this discovery were rewarded in less than a year by a litter of eight dead-born pups from bitch 127. (See full history.) The thyroid lobes of these pups were connected by a very short, thin isthmus, and were at least twelve times as large as normal.

Later a third litter of five pups, presumably at first from unoperated parents, was discovered in the kennels of the laboratory by the janitor, John Schutz, to whom I am greatly indebted for most intelligent assistance in my experimental work. The thyroid lobes of these pups were, much to my surprise, almost as large as the thyroid lobes of the pups of bitch 127, and for a short time our theory seemed to be insecure. Upon investigation, however, we found that the mother of the pups had been twice operated upon. The first operation was a laparotomy for the introduction of a syringeful of a bouillon culture of staph. aureus into the abdominal cavity. A few months later the left thyroid lobe of this bitch had been excised, and found on microscopical examination to be hypertrophied. Impregnation occurred after the excision of the left lobe of the thyroid gland. The bitch was killed soon after the pups were whelped, and the above facts verified by the autopsy. The right lobe showed an advanced stage of hypertrophy.

We were, accordingly, so fortunate as to have three litters of puppies from bitches deprived in part of the thyroid gland. Bitch 97 was impregnated by dog 90, after his left and two-fifths of his right lobe had been excised. The other two bitches were impregnated by normal dogs. The thyroid glands of the puppies of bitch 97 were much larger than the glands of the puppies of the other litters. The former were, as I have said, about twenty times as large as our largest normal gland of a puppy at birth, whereas the latter were only twelve and ten times as large as they normally should be. In the minute structure, too, the former differed somewhat from the latter; for there was absolutely no colloid, and rarely a trace of a vesicle in the very large glands of the former, while in the latter there were still a very few vesicles and still occasionally a trace of colloid. The normal gland of a puppy at birth has many acini filled with colloid, but they are much smaller and much less preponderant than in the adult gland. The epithelium is much higher and the colloid much thinner in the puppy's than in the adult gland.

The structure of these greatly hypertrophied glands of puppies resembles closely that of the glandula parathyroidea.

It occurred to us, naturally, to inquire whether hypertrophy of the thyroid lobes might not occasionally exist in dogs whose neck had not been molested. I excised, accordingly, the left lobes of five dogs into whose abdominal cavities some months previously syringefuls of a bouillon culture of staph. aureus had been introduced. The thyroid lobes of four of these dogs were hypertrophied.

The lobes of a dog which had fallen from the third-story window of the laboratory were hypertrophied.

Those of a dog which had just recovered from pneumonia were hypertrophied and most of the follicles were filled with cells, whereas those of a dog which had died of pneumonia were normal.

The thyroid glands of two dogs which had been confined for a long time in the laboratory were not hypertrophied.

Dog 136 was inoculated, February 4, 1890, with diplococcus pneumoniæ. Fourteen days later the left thyroid lobe was normal.

Dog 151, March 3, 1890. Excised the greater part of the left humerus for blood clot experiment. Dead space allowed to fill with blood. March 24, three weeks later, anæsthetized to death. Advanced hypertrophy of thyroid gland.

The janitor, John Schutz, who, as I have said, took a most intelligent interest in these experiments, examined for us the thyroid lobes of one hundred dogs in the city pound. Certainly one and probably two of these dogs had hypertrophied glands.

The left lobes of the dogs used for complete or piecemeal extirpation experiments were without exception, on microscopical examination, found to be normal.

The value of the closed wound experiments may well be questioned, for it will be observed that most of the dogs with closed wounds and plaster of Paris dressing died sooner or later, irrespective of the experiment. The one-sided transplantations and isolations, for example, resulted eventually in the death of the animal. These experiments should not ordinarily have been fatal. In some instances pneumonia, perhaps due to distemper, was the immediate cause of death. But in most cases the dogs died with a peculiar scurvy-like cachexia, to which most of the dogs with closed wounds and plaster of Paris dressing during the year 1888 succumbed.

Hence we cannot consider the question as to the possibility of transplanting the thyroid lobe into the neck of another dog as posi-

tively settled. We cannot account satisfactorily for the peculiar scurvy-like cachexia which so many of the dogs with closed wounds developed. I am inclined to suspect that it may have been due in some way to the confinement caused by the dressing. The wounds were covered with a large pad of horse-hair, and this was held in place by a plaster of Paris bandage which immobilized to a certain extent the neck and the forelegs of the dogs.

Not one of the many dogs with open wounds developed this peculiar condition, nor did one of them die until enough, and usually more than enough, of his thyroid lobes had been excised to account satisfactorily for his death.

On September 20, 1888, Dr. Welch kindly presented at the meeting of the Association of American Physicians in Washington, an abstract of my experimental work on the thyroid glands of dogs and described the hypertrophy of these glands, upon which especial emphasis was laid. He demonstrated microscopical sections of the glands, and reported regarding the histological changes characterizing the hypertrophy and the conditions under which hypertrophy was observed. Dr. Welch's remarks on this subject were published at the time,* but they have escaped the notice of subsequent writers. Our published observations concerning hypertrophy of the thyroid gland, which will now be described in detail, date from the year 1888.

Before the first publication of my results in 1888 there was little evidence that after extirpation of a part of the thyroid gland the remainder hypertrophied.

Horsley† and Wagner‡ were the only ones who thought that they had observed hypertrophy of one lobe after excision of the other. Wagner's testimony was supported merely by his belief that in two instances the remaining lobe was larger than the one first extirpated; but Horsley had with the microscope observed changes which were described as follows: "The acini were found to undergo very remarkable changes. The epithelial cells lining them multiplied in number and increased in size, so that there was a plication of the acinal

* The New York Medical Record, 1888. The Medical News (Philadelphia), 1888.

† Horsley: The Pathology of the Thyroid Gland, Lancet, Dec. 18, 1886.

‡ Wagner: Ueber die Folgen der Exstirpation der Schilddrüse nach Versuchen an Thieren. Wien. Med. Blätter, 1884, Nos. 25 and 30.

wall. The full reason for this folding was not clear. There was no increase in the number of the parenchymatous cells of Weber, and no metamorphosis of the embryonic tissue into acini. The colloid material did not increase in amount, but changed in consistence, became softer, more viscous and less solid, so that at one time it appeared like a network of viscosity, and later on had a watery aspect. Increased activity of the organ appeared therefore to cause a diminution in the consistence, and this was contrasted with the greater solidification of the acinal contents that occurred when the function was less active." "If the animal wasted after the removal of the lobe of the thyroid gland, then there need be, and probably would be, no hypertrophy of the remaining lobe." Horsley gives Lorenz credit for insisting on the importance of this matter of weight in determining hypertrophy, and has himself observed that if one kidney is excised and the animal loses in weight, the other kidney does not hypertrophy. I am not sure that this statement should not be reversed. I believe rather that the loss of weight was due to the fact that the remainder of the gland did not become hypertrophied, than that the absence of hypertrophy was caused by the loss of weight.

Fuhr* affirmed unreservedly that the observation of Wagner as to the hypertrophy of the remaining portion of the gland was disproved by his experiments and by those of Sanguirico and Canalis.†

To determine this point, Fuhr made six experiments. 8, 25, 27, 28, 33, and 41 days intervened between the first operation when one lobe or parts of both lobes were removed, and the second operation when the remainder of the gland was excised. A glance at my table of hypertrophies (Table IV) will perhaps explain how it could happen that Fuhr did not in these experiments obtain hypertrophy of the thyroid gland.

* Fuhr: Archiv für experimentelle Pathologie, No. 21, 1886, p. 449.

† Sanguirico and Canalis: Première communication préliminaire. Archives Italiennes de Biologie, T. V, 1884, p. 390. These investigators extirpated one entire lobe and the superior two-thirds of the other lobe of two animals. Both animals died, one on the third day, the other on the sixth day. The remaining pieces, as we should expect, showed no change; the time was too short for the development of hypertrophy. In two instances they extirpated one lobe and the inferior two-thirds of the other lobe. Both animals lived. The remaining piece was not examined in either case.

With two exceptions I did not encounter advanced hypertrophy until after the 43rd day. Fuhr might nevertheless have had hypertrophy in every case except the one in which only eight days intervened between the two operations, and we might have expected it in the 41-day case. The fact that hypertrophy did not occur in this last case was probably due to the nature of the experiment; for all of the arteries and veins at the hilus of both lobes were ligated and the upper poles of both lobes exsected.

Mr. Horsley was in America in 1889 and it gave me pleasure to show him my specimens. In 1891, in his famous article on the function of the thyroid gland,* he very courteously declines to say anything about the microscopic changes in the hypertrophied thyroid gland, and refers for this to my work† which was to have been published four or five years ago.

Notwithstanding the fact that Dr. Welch, in his abstract of my work on hypertrophy, described more than seven years ago the principal changes in the structure of the gland, subsequent writers and investigators do not seem to suspect that a structural change is to be looked for in hypertrophy of the thyroid gland. Nor has any one observed the hypertrophy which almost invariably takes place in the remaining thyroid lobe within perhaps 40 days of the time of the removal of the other lobe. The isolated observations of Wagner and Horsley are referred to with scepticism or are discredited, and my work seems to have escaped observation. von Eiselsberg‡ performed on two cats extirpation of both lobes in two acts. Seven and fourteen days intervened between the acts in these cases. That hypertrophy of the remaining lobe might not take place we can readily understand; the time was almost too short. He believes, however, that there was "évidente hypertrophie" in four of fourteen transplantation experiments. I am inclined in this instance to doubt the observations of this excellent investigator, because (1) he trusted to naked eye appearances, and (2) the time which elapsed from

* Horsley: Die Function der Schilddrüse; eine historisch-kritische Studie. Internationale Beiträge zur wissenschaftlichen Medicin (Festschrift, Rudolph Virchow, gewidmet), Bd. I, p. 369.

† Horsley: *loc. cit.*, p. 387.

‡ Anton Eiselsberg: Ueber Tetanie in Ausschlusse an Kropfoperationen. Wien, 1890, Alfred Halden.

the removal of the first lobe for transplantation to the removal of the second was too short (3, 4, 4, 11, 11, 14, 15, and 15 days) for the development of this hypertrophy. The diagnosis of hypertrophy cannot be made with the naked eye. There are certain structural changes which are uniform and constant in hypertrophy and without which we cannot venture to assert that it is present. Even if there were no changes in structure, the naked eye, handicapped by memory, might easily make a wrong estimate as to size. Furthermore, an absolute increase in volume and weight might be due alone to tissue infiltration. Hypertrophy of the thyroid without change of structure at some period of its evolution is, as I have said elsewhere, inconceivable. Apparently the only observations of von Eiselsberg in this series which were controlled by the microscope were the only ones in which he would have been at all likely to encounter hypertrophy, and in these he says it was not present. I refer to two cases in which the intervals between the operations were 21 and 115 days. von Eiselsberg's description of the microscopic appearances in the latter case interests me very much. He describes conditions which in the dog would indicate hypertrophy—at least an early stage of it.

He says, "The injected material (artificial injection of the blood-vessels) penetrated everywhere even into the transplanted (between peritoneum and fascia) gland in which, as in normal animals, the dendritic branching of the vessels could be observed." "In some places the colloid degeneration which often occurs normally was to be found in the interior of the vesicles." This dendritic branching of the blood-vessels is one of the characteristic structural changes in the hypertrophied gland of the dog, and produces or keeps pace with the production of the involutions into the follicles. What von Eiselsberg designates as colloid degeneration is possibly the change in the colloid which we always observe in hypertrophy. It becomes thin and vacuolated, and after a time disappears entirely.

Wagner* is regarded as the authority for the generally accepted notion that the thyroid gland hypertrophies after a part of it has been removed. In support of his views he has only two observations to offer, one upon a dog and one upon a cat. In the case of the dog, 35 days intervened between the first and second operations. The lobe

* Wien. Med. Blätter, No. 30, p. 932.

which was supposed to be hypertrophied had 35 days for the development of the hypertrophy. Wagner does not give the date of the second operation upon the cat, hence we do not know how long a time the cat's thyroid had in which to become hypertrophied. We know (see Table No. IV) that hypertrophy is possible in 15 days, but we consider such early hypertrophies as exceptional. It is more than probable that Wagner observed hypertrophy in the case of the dog, although a microscopic examination of the gland was not made. His description of the enlarged thyroid arteries is quite convincing. I have repeatedly made the same observation, viz. that the thyroid blood-vessels, arteries and veins, of the hypertrophied lobe seem to be dilated or enlarged. But one cannot make a positive diagnosis of hypertrophy from the naked eye appearances. At one time, after considerable practice, I thought that I could, without the microscope, diagnosticate the existence of hypertrophy, but I discovered subsequently that my diagnosis was fallible. I believed that a certain succulence, due, so I thought, in part to the high epithelium and perhaps principally to an increase in vascularity, was characteristic of hypertrophy, particularly when at the same time the color of the gland indicated an unusually great blood supply. But I have found microscopic evidence of advanced hypertrophic changes in glands that seemed to be unusually hard and that looked more anæmic than the normal gland. Hence the microscope must, as I have said elsewhere, be our criterion of hypertrophy.

The Structure of the Hypertrophied Thyroid Glands.

In the normal gland of the dog the follicles as they appear in section vary in size more than in shape. They incline to roundness in shape, are lined by a single layer of cubical, sometimes almost flat epithelium, and are filled with an apparently homogeneous substance called colloid. This colloid material is semi-solid in the normal gland and seems to distend the follicles. Even in the hardened specimen a cleft between the colloid and the cells which line the follicle is exceptional.

The thyroid gland is richly supplied with blood-vessels. Each follicle is embraced by a vascular network. The distribution of the small vessels and capillaries assists one greatly in the interpretation

of the minute anatomy of the hypertrophied gland. Even in the normal gland the blood-vessels sometimes unravel an interfollicular puzzle. They indicate, for example, the primitive follicles where they surround a few epithelial cells, and sometimes in this way they differentiate for us epithelial cells in what might otherwise seem a jumble of interfollicular cells without arrangement (see Fig. 6, Plate X).

We look to the epithelium (perhaps also to the colloid) for the first indication of hypertrophy, and sometimes find in one gland all of the stages of transition from low cubical to high cylindrical epithelium. How rapidly these changes may take place we cannot as yet say. Coincident with the increase in the height and breadth of the epithelium are changes in the colloid material and in the shape of the follicles. The follicles lose their roundish form and acquire increasingly irregular contours. Little bud-like processes sprout from the walls of the follicle. These sprouts seem to be a folding in (involution or plication) of the wall. The circumference of the follicle necessarily increases to accommodate the epithelium as it becomes broader. If the formation of normal colloid kept pace with the changes in the epithelium we might expect to have tremendous follicles still distended with colloid and retaining their more or less circular shape. But the colloid substance vanishes as the hypertrophy advances. It becomes vacuolated and apparently very thin, and eventually disappears or is represented by a delicate reticulum (see Fig. 2, Plate IX, Fig. 8, Plate X and Photo. V).

There seems to be no intrafollicular resistance. The wall of the follicle, very much longer than it was when lined with low epithelium, accordingly becomes folded upon itself. Little undulations and buds and digitations, short and long, appear. These involutions or digitations are oftener simple than compound. Sometimes they have several processes or branches. The shape of the central cavity of a follicle is the reverse cast, we may say, of its involutions. It is often roughly star-shaped. Sometimes it is like a bay with many short branching estuaries. In the very advanced hypertrophy the central cavity and its ramifications are pressed, so it seems, into elongated channels. These channels are often reduced to scarcely recognizable slits. It is then sometimes easier to differentiate the original follicle by the interfollicular blood-vessels than by the intrafollicular

canals. The central axis of each involution is occupied by blood-vessels. The change backwards from hypertrophy to normal would be a simple matter. The shrinkage of the epithelium, the atrophy of the new—if indeed they are new—blood-vessels, and the formation of normal colloid, would accomplish the transition.

Hypertrophy. The Time required for its Development.

In my second dog, and 71 days after excision of the left lobe, hypertrophy was discovered. One could not have failed to be surprised at the great size of the right lobe, which weighed 2.5 grm., or more than four times as much as the left, the weight of which was 0.6 grm. The right lobe showed the histological and morphological changes which we soon learned to recognize as an advanced stage of hypertrophy. Not a vestige of normal thyroid structure remained.

Only a few of my experiments were made solely to determine the time required for the production of hypertrophy after excision of one lobe. Nevertheless we have a sufficient number of observations to justify the statement that if one thyroid lobe be excised in whole or in part, or mutilated, however slightly, hypertrophy of the other lobe will, to a greater or less degree, almost surely supervene within 40 days, and sometimes much earlier than this.

To estimate the time required for the development of the hypertrophy we must exclude, I am convinced, most of the dogs whose wounds were closed and then dressed with a plaster of Paris bandage—a bandage which, as I have explained, encircled the neck and confined the shoulders and upper part of the forelegs. The operations upon the dogs so treated were as follows: thirteen isolations of the left lobe, or one-sided Munk's operations; four extirpations of the left lobe followed immediately by substitution transplantations;* one manipulation enucleation† of the left lobe, and one extirpation of the left lobe.

The wounds healed absolutely per primam‡ in all of the cases except

*The lobes of two dogs are exchanged and transplanted accurately *in situ*.

†The gland is raised out of its bed somewhat roughly, its loose connective tissue attachments are torn through, and it is then dropped back into place. Its principal blood-vessels are not injured.

‡I attribute the excellent results in wound-healing to the buried skin suture, "subcuticular suture." Only a small proportion of my wounds in

two (dogs 48 and 69). In one of these cases (dog 69) the suppuration was entirely superficial and very slight. Nevertheless most of the nineteen dogs so treated (closed wounds and plaster of Paris dressings) developed soon after operation peculiar symptoms and died, whereas the dogs with open wounds were perfectly well even when reduced to one-fourth and less of the thyroid gland (vid. Tables III and IV). The most striking symptoms which the dogs with plaster of Paris dressings developed were a profound anæmia, a peculiar scurvy-like condition of the gums and a falling out of the hair. The dogs would become exceedingly anæmic a few days after the operation, and within a week or ten days of the operation the affection of the gums would manifest itself. This scurvy-like condition of the gums was so severe in several instances that the body of the lower jaw was entirely denuded except at its lower border. An excessively foul-smelling breath accompanied this condition of the gums. Nine of these dogs died within twenty-five days (vid. Table IV): on the 15th day 1, on the 17th day 1, on the 18th day 2, on the 20th day 3, on the 24th day 1, on the 25th day 1. The right lobes of the nine dogs obtained post mortem showed, with two exceptions (dogs 58 and 68),* no perceptible change in structure, but the follicles of these glands were in greater part filled with cells—cells which clearly had their origin in the epithelium which lined them. Another dog of this group (No. 72) which died on the 39th day with the same symptoms had a thyroid gland (right lobe) which showed the described change—follicles filled with cells.

dogs healed before I devised this suture. To take the stitches, the needle is first passed into the under surface of the skin as near to the deeper angle of its cut edge as possible, and including only the deeper layers of the skin, is made to emerge in the same plane. Sebaceous follicles and hair follicles should not be perforated by the stitches. We now use the continuous, buried skin suture in preference to the interrupted suture. Knots are unnecessary, because the tissues hug the uninterrupted suture so closely that slipping does not occur. Long ends of the uninterrupted silk or silver suture emerge at the angles of the wound, to make easy its withdrawal at the end of ten days or two weeks. If catgut is used the suture is not, of course, withdrawn, and may be tied. This suture was first described in the Johns Hopkins Hospital Bulletin, Vol. 1, p. 13.

*Dog 58, early stage of hypertrophy on 15th day. Dog 68, early stage of hypertrophy on 25th day.

These ten cases died from the isolation or extirpation of one thyroid gland, which under ordinary conditions are harmless procedures. The profound anæmia, the scurvy of the gums and the sudden and very rapid falling out of the hair must be ascribed, I believe, as well as the fatal results, to diminished functional activity of the remaining lobe of the gland. A perverted functional activity is indicated perhaps by the proliferation of the cells of the follicles.

Of the nine remaining cases of this plaster of Paris group, one (dog 56) died on the 65th day. Four days after the removal of the left lobe he developed the tongue tremor, which is always seen when both lobes have been extirpated. This tremor subsided in two or three days. But already a conjunctivitis and central corneal ulcer of the left eye had developed. Within a month the dog became exceedingly anæmic; his gums were discolored at the edges, separated from the jaws, and beginning to slough. Before his death there was complete loss of hair. It is to be observed that this dog soon after the first operation had symptoms of extirpation of both thyroid lobes, that he recovered from these and lived altogether 65 days after the operation. The right lobe, obtained post mortem, was unmistakably hypertrophied to a certain extent (see Table IV); the epithelium was cuboidal or cylindrical, and the follicles were somewhat angular and contained the thin reticulated colloid material.

Seven dogs of the plaster of Paris group recovered perfectly from the operation: four (77, 43, 55, 2) without, at any period, a symptom; three (69, 70, 45) with temporary symptoms of thyroid privation. The remaining lobes of all of these seven dogs were hypertrophied to an advanced degree. One dog (67) of this group remains to be considered. He had not been well at any time since the first operation, and was very much emaciated when, on the 61st day after the first operation, the right (remaining) lobe was removed. The right lobe was perfectly normal. It was not hypertrophied, as we should have expected it to be had the dog made a good recovery from the first operation, nor were its follicles filled with cells, as we might, possibly, have expected them to be if the dog had died from the first operation. It is evident, therefore, that to estimate the time required for the development of the hypertrophy, we must exclude most of the dogs whose wounds were closed and dressed with a plaster of Paris bandage. Four of these dogs, however, as we have seen, made a

perfect recovery from the first operation and without a symptom of thyroid privation.

Including these four we have thirty-six unquestionable observations on which to base our conclusions: dogs 116, 110, 118, 120, 121, 108, 119, 124, 88, 125, 122, 123, 112, 93, 92, 109, 87, 81, 86, 105, 83, 77, 103, 96, 43, 55, 2, 91, 104, 84, 82, 90, 94, 85, 126, and 127 (see Table IV).

Three hours was the shortest interval between the first and second operations, and 152 days the longest. The intermediate intervals were 24 hours, 4 days, 7 d., 7 d., 10 d., 10 d., 13 d., 15 d., 17 d., 19 d., 19 d., 22 d., 26 d., 42 d., 43 d., 49 d., 50 d., 50 d., 51 d., 53 d., 56 d., 57 d., 63 d., 67 d., 69 d., 70 d., 71 d., 71 d., 82 d., 82 d., 85 d., 95 d., 104 d., 132 d., 132 d. No change was observed until the seventh day, and this was a barely perceptible change (vid. dog 120, Table IV). It was observable in one only of the two seven-day observations. In one of the two ten-day observations an undoubted but very slight increase in the height of the epithelium was noted. On the 15th day quite advanced hypertrophy followed the extirpation of the inferior half of the left lobe.* An early stage of hypertrophy of both lobes on the 17th day followed ligation of everything at the upper poles except the arteries. We have two right lobes removed 19 days after the extirpation of the left lobe. One is normal, the other is very slightly hypertrophied (vid. Table IV). On the 22nd day after extirpation of the left lobe we find a normal right lobe. A perfectly normal remaining lobe later than 22 days after extirpation or isolation of the first we have not seen.†

The specimens of the 26th, 42nd, and 43rd days show early hypertrophy. Dog 92, from which the 42-day specimen was taken, furnished a most interesting piece of thyroid tissue at the unexpected autopsy. The first operation on this dog was the extirpation of the inferior half of the left lobe. Forty-two days later, the dog being apparently perfectly well, the remainder of the left lobe and the inferior half of the right were removed. These pieces we must remember were very slightly hypertrophied, although not apparently

*One of the dogs dressed with plaster of Paris also showed an unmistakable hypertrophy on the 15th day.

†Dog 67 is the only exception, and this we have excluded for reasons already given.

increased in size. The epithelium was higher than that of the piece excised at the first operation (the inferior half of the left lobe), but the colloid was still present in its usual form; there were no involutions, and the shape of the follicles was not much changed—on the whole, then, only a feeble or unsuccessful attempt at hypertrophy. As a rule, a dog not only survives this second operation, but has no symptoms of thyroid privation from it. Dog 92, however, died within four days of the second operation. The remainder of the thyroid gland, the superior half of the right lobe, obtained at the autopsy, presented the picture with which we have become so familiar in the dogs with closed wounds and plaster of Paris bandages, which died after extirpation or isolation of one lobe. The follicles were everywhere completely filled with disarranged cells, cells which had evidently been rapidly proliferated. The original follicles could be traced with difficulty and, as a rule, only by the blood-vessels. There was no evidence of an advance towards a true hypertrophy.

Dog 96 furnishes another specimen of this peculiar change, which for the present we designate merely as follicles filled with cells. In this instance the superior half of the left lobe was removed. The wound was left open. The dog was apparently perfectly well for about 40 days, then became sick and died on the 63rd day after the operation. The right lobe was tremendously hypertrophied, weighing 3.6 grms. With the microscope, the changes which indicate advanced hypertrophy were present, and in addition the follicles and the follicular channels* were filled with cells.

We are convinced that this apparently rapid proliferation of cells within the follicles cannot be a post-mortem change. It is inconceivable that such striking morphological changes should be accomplished by post-mortem cell exfoliation. There seems to be a great increase in the number of the cells in the cases under consideration. Furthermore, these experiments were, for the most part, conducted in winter and many of the autopsies were made soon after death. All specimens obtained later than 43 days after the extirpation of the whole or one-half of one lobe showed without exception the changes which we designate as advanced hypertrophy. In two instances (dogs

* In the very advanced stage of hypertrophy the follicles, as I have said, have lost their circular outline on section, and are drawn out into fantastic shapes and channels.

103* and 104) manipulation enucleation, accomplished without injury to the principal arteries and veins of the gland, was followed by hypertrophy of both lobes in 57 and 82 days after the experiment.

A ligation of everything at the upper poles of both lobes except the principal arteries (dog 105), produced no structural changes in the gland in 51 days.

Ligation of the left lobe 2 or 3 mm. above the inferior tip was practiced twice (dogs 126 and 127).† One hundred and thirty-two days after this experiment the left lobe and a portion of the right (inf. $\frac{1}{3}$) were removed from each of the dogs, and found in one (126) to be fully hypertrophied and in the other (127) to be perfectly normal.

In March, 1895, Gley‡ described certain cellular changes which take place in the "glandules thyroidiennes" after thyroidectomy in the rabbit, and wonders if the observed changes are to be considered as transitional and as the first phases of an evolution which will ultimately give to the entire glandule the structure of the thyroid gland. He and Nicolas have been more fortunate than others, if they have observed in two cases (6 and 7 days after thyroidectomy) karyokinetic figures§ in the glandules thyroidiennes. It had, they say, for some time been considered that the glandules became hypertrophied after thyroidectomy, but no one hitherto had succeeded in discovering any histological changes or positive multiplication of cells to explain an increase in the size of the glandules. Our observations on hypertrophy would lead us to believe that whatever the final change in the glandules thyroidiennes (parathyroid glandules) after thyroidectomy might be, the transformation to follicles filled with colloid would certainly not be an early manifestation. The colloid

* Notwithstanding the apparently tremendous hypertrophy, dog 103 died with typical symptoms of thyroid privation. The increase in the size of the thyroid lobes in dogs 103 and 104 was due in part to parenchymatous hemorrhage. See full histories in text.

† The history of both of these dogs is given in full in the text. See also foot-note, page 386.

‡ Primières résultats de recherches sur les modifications histologiques des glandules thyroidiennes après la thyroidectomie. E. Gley and Nicolas, Comptes Rendu Hebdom.

§ I have observed very few karyokinetic figures, even in the thyroid gland, although most of my glands were hardened in Flemming's sol. stained with safranin, and carefully studied for mitosis.

material is possibly a reserve secretion which is called upon to supply the requirements of the organism so soon as it is deprived of a part of the gland. If this is so, the balance is not under all circumstances nicely adjusted, for cutting off the tip of one lobe stimulates to tremendous hypertrophy of both the lobes and the accessory glands and exhausts the reserve supply of colloid. It is accordingly conceivable that a transient auto-intoxication* might be caused by resection of a small portion of one lobe or by any manipulation which would induce hypertrophy. It is doubtful, however, if we should be able ordinarily to detect this intoxication, inasmuch as the hypertrophy and the coincident resorption of colloid take place as a rule so very slowly. In some dogs, however, hypertrophy develops quite rapidly, and in all the disappearance of the colloid is perhaps the earliest change.

I have said that the greatly hypertrophied glands of the puppies of parents deprived in part of the thyroid glands bear a striking resemblance in structure to the parathyroid glandule of dogs. In some instances it seems to be impossible to distinguish the one from the other.† The enormously hypertrophied thyroids of the puppies of bitch 97, for example, have neither colloid nor acini nor solid follicles, and present a structure which is, so far as one can judge from the specimens which I have preserved, identical with that of the parathyroid glandule.‡ Both parents of these puppies had been deprived in part of their thyroid gland. In the two instances in which only the female parent was subjected to a partial thyroidectomy, the hypertrophied glands of the puppies had still in some places small follicles filled with colloid, but for the most part there was little left to remind one of the original structure. It happens, fortunately, that the parathyroid glandule appears in several of my sections of normal and hypertrophied thyroid glands of adult dogs. I can therefore assert quite positively that no structural change took place in this glandule after partial extirpations of the thyroid lobes.

Furthermore I cannot believe it to be a fact that dogs regularly survive the removal of the entire thyroid gland provided that the

*Could resorption of this material during the operation explain some of the many deaths which occur during or soon after operations for exophthalmic goitre?

†I attach little, if any, importance to this resemblance of the greatly hypertrophied glands of the new-born puppies to the parathyroid glandules.

‡Photo. I shows parathyroid glandule magnified 40 diameters.

"glandules thyroidiennes" (parathyroid glands) are enucleated and left in place—to say nothing of the difficulty of such an experimental feat.

DESCRIPTION OF THE PHOTOGRAPHS. THYROID GLANDS OF DOGS.

Photo. I. 40 diameters. Normal gland. Shows a parathyroid glandule near the hilus of the lobe. Just at this point one sees the projection inwards of the delicate capsule of the lobes, embracing first the parathyroid lobule and then supporting the large blood-vessels. The follicles are filled with the colloid material and are lined with a single layer of low cuboidal epithelium. In a few of the follicles, particularly the larger ones, the colloid material has apparently contracted and drawn away from the epithelium. As a rule the follicles are not merely filled, but seem to be distended with colloid.

Photo. II. 275 diameters. Normal thyroid gland. Shows in the centre one of the more solid and so-called interfollicular portions of the gland. The cells of the interfollicular portion are for the most part epithelial and are grouped like young or very small follicles with little or no colloid. The long nuclei of the minute blood-vessels assist one to differentiate the immature or interfollicular follicles.

Photo. III. 275 diameters. Early stage of hypertrophy. High epithelium, rarefied (vacuolated) colloid. Angular follicles. In centre solid area of gland.

Photo. IV. 275 diameters. Right thyroid only 17 days after excision of left. Hypertrophy more advanced than in Photo. III. Epithelium already cuboidal in most follicles. The vesicles are irregular in shape. The irregularity is due to a tendency to wave involutions. The colloid substance is abnormal. The nuclei of the blood-vessels well shown in this photograph.

Photo. V. 275 diameters. The follicles, except the central one, are almost completely filled by the involutions of the high (cylindrical) epithelium. The epithelium may be traced uninterruptedly from involution to involution. In this section the vessels have, for the most part, been divided transversely. They are easily recognizable at the bases of the involutions of the central follicle by the long

nuclei. In several of the vessels blood corpuscles are to be seen. The colloid material is reduced to little more than vacuoles and a reticulum. The central cavities in this stage resemble very irregular bays with numerous estuaries, single, bifurcated, trifurcated, etc.

Photo. VI. 275 diameters. Inferior half of right thyroid. Dog 92. An almost normal gland; but probably a very early stage of hypertrophy 42 days after resection of inferior one-half of left. The shape of the follicles and the higher epithelium indicate beginning hypertrophy.

Photo. VII. 68 diameters. Superior half of the right lobe of dog 92. The inferior half of the very same lobe removed only four days previously is shown in Photo. 6. The dog died very unexpectedly after the removal of the remainder of the left lobe and the inferior half of the right lobe. The wound, treated by the open method, was healthy. Aside from the inflammation the change in the gland is most striking. The follicles are completely filled with cells. These cells are evidently of epithelial origin and were proliferated or exfoliated in four days at most.

Photo. VIII. 275 diameters. From one of the cases with closed wound and plaster of Paris dressing. Follicles filled with cells.

Photo. IX. 12 diameters. Normal gland of new-born puppy, shows two accessory lobules. The one which projects so prominently from the surface is a so-called parathyroid glandule. The other, adjoining and to the left of the first, is thyroid tissue, but without colloid.

Photo. X. 12 diameters. Hypertrophied gland of new-born puppy of dog 97. About twenty times as large (both lobes) as normal gland.

DESCRIPTION OF THE PLATES. THYROID GLANDS OF DOGS.

Plate IX, Fig. 1. 90 diameters. Normal gland. Gives the correct idea of the shape of normal follicles. Most of the follicles are filled with colloid. Some are empty. The epithelium is flat.

Fig. 2. 530 diameters. Two follicles of a hypertrophied gland. The epithelium is cylindrical and in places several rows deep. The colloid material is replaced by vacuoles and a reticulum. The follicles are distinctly defined by the long nuclei of the blood-vessels.

Fig. 3. 530 diameters. One follicle of normal thyroid gland of dog. The orange color indicates blood.

Fig. 4. 925 diameters. A portion of central canal of hypertrophied follicle, with longitudinal or slightly oblique section of involution on the right hand, and transverse sections of involutions on the left. The blood discs in orange indicate the situation of the capillaries.

Plate X, Fig. 5. 240 diameters. Injected specimen. Hypertrophy. The injection has reached the terminal ramifications of the blood-vessels in the involutions. In several instances the follicles are seen to be almost completely surrounded by blood-vessels. The epithelium is cuboidal. The colloid is replaced by the reticulum.

Fig. 6. 240 diameters. Injected specimen. Hypertrophy. A more solid part of the gland which might be called (erroneously) interfollicular were it not for the injection. The injection defines follicles which have no central canal and which might be termed solid. It also differentiates the intra- from the interfollicular spaces. Compare with Fig. 7.

Fig. 7. 240 diameters. Hypertrophy. Same stage as Fig. 6. Designed to show the solid and very advanced stage of hypertrophy. The nuclei of the blood-vessels have unintentionally been omitted by the artist. It is interesting to note the confusion caused by the omission. Compare Fig. 6.

Fig. 8. 240 diameters. Advanced hypertrophy. Natural injection indicated by daubs of orange. One large and ten or twelve small follicles. Colloid replaced by reticulum in all the follicles.

Fig. 9. *a*. Usual size of one lobe of dog's thyroid at birth as estimated from three litters of puppies (from 15 to 18 puppies).

c. Actual size of thyroid gland of puppy whelped by bitch No. 97 when she had been deprived of her left lobe, and sired by dog No. 90, whose thyroid had been reduced to two-thirds of one lobe. See history of No. 97.

b. Left lobe of dog No. 3. Actual size.

d. Hypertrophied right lobe of same dog (No. 3). Actual size.

Addendum.

After receiving the page-proof of this article I had the good fortune, thanks to the courtesy of Dr. Abel, to make an autopsy

upon a dog whose thyroid lobes had been removed *in toto* by him just a year ago. The dog emaciated rapidly after the loss of the thyroid gland, became profoundly anæmic, lost most of his hair,* seemed to suffer from a more or less constant itching, and developed by scratching a dermatitis which in some places might have suggested myxœdema. He never developed convulsions or tetany or tremors or any of the more pronounced symptoms of complete extirpation. Neither did he suffer from the scorbutic gingivitis which I have described as occurring in a special group of my cases.

He was fed with thyroid glands or thyroid extracts for 2 months, but not with any very appreciable effect. The autopsy was not performed until about 30 hours after the death of the animal.

Autopsy. Small dog seven years old, much emaciated and almost hairless. No lesions of the viscera macroscopically discoverable. The neck was dissected with great care. The thyroid lobes had undoubtedly been removed; not a trace of them remained. An accessory thyroid which is usually found behind the hyoid bone, on the thyro-hyoid membrane, was apparently wanting. This gland had been searched for by me during the life of the dog, but could not be found.

In the neighborhood of the arch of the aorta three or four very minute reddish-brown bodies were discovered which proved to be epithelial bodies, almost if not precisely identical in structure with the so-called parathyroid glandules. These little bodies were certainly not much more than one-quarter the size of the head of an ordinary pin. Under the arch of the aorta and very near the ductus Botali were three very large accessory thyroids, two of them as large as a very small pea. The three accessory thyroids weighed together .08 gramme. After examining with the microscope a number of sections of these accessory thyroids, I was impressed with the simplicity of their structure. Most striking was the fact that there were very few interfollicular cells. Almost all the cells were engaged in the formation of follicles, and all of the follicles seemed distended to their utmost with apparently normal colloid. The cells lining the follicles (and there seemed, as I have said, to be

*This dog was supposed to have mange before he was operated upon. The loss of hair and the dermatitis were perhaps due to this skin disease.

very few other cells) were a little higher than normal. There were rather numerous little epithelial buddings into the follicles, and in some of the buds blood-vessels could be demonstrated.

We may assume with considerable confidence that these aortic accessory thyroid glands have passed through the changes which we describe as hypertrophic. Hypertrophy of the thyroid as we have represented it is probably a transition stage—transitional to the condition which makes possible the greatest fulfilment of functions in some (*i. e.* Dr. Abel's dog) and a greater activity in all cases. How then shall we interpret what we see in these greatly enlarged aortic thyroids? The enlargement, it would seem, must be due in this instance either to an increase in the size of the original follicles or to an increase in the number of follicles containing colloid, or to both. It cannot be due alone to the inconspicuous increase in the size of the cells. This increase in the size of the follicles and in the number of follicles containing and distended with colloid implies not only a greater amount of colloid, but also either a greater number of cells than the gland originally contained, or a rearrangement of the original cells.

TABLE I.—*Extirpation of Both Lobes.*

No. of Animal.	Description of Animal.	Date of Operation.	Treatment of the Wound.	Healing of the Wound.	Weight of the Lobes.	Date of Death.	Autopsy.	Remarks.
1. (30).	Medium sized old dog.	1, III, 1888.	* Buried skin sutures.	Per primam.	Left, 0.7 grm. Right, 0.7grm.	7, III, 1888.	Negative.	Developed double conjunctivitis. Died with typical symptoms.
2. (31).	Medium sized old bitch.	1, III, 1888.	* Buried skin sutures.	Per primam.	Left, 2. Right, 2.	8, III, 1888.	Negative.	Typical symptoms.
3. (32).	Small young dog.	1, III, 1888.	* Buried skin sutures.	Per primam.	Left, 1. Right, 1.	17, III, 1888.	Negative.	Double conjunctivitis. Typical symptoms. Killed when nearly dead, to obtain fresh tissues.
4. (39).	Medium sized dog.	3, III, 1888.	* Buried skin sutures.	Wound apparently not infected. Too early for union.	Both lobes very small and pale.	5, III, 1888.	Negative.	Typical symptoms.
5. (40).	Small dog about 1 year old.	5, III, 1888.	* Buried skin sutures.	Per primam.	Left, 0.35. Right, 0.15. (Unusually small lobes.)	13, III, 1888.	Negative.	Dog not observed by me for the five days preceding his death.

* Antiseptic precautions, closed wound and plaster of Paris dressing.

TABLE II.—*Isolation Experiments (Munk's Operation).*

No.	Description of Animal.	Date of Operation.	The Treatment of the Wound.	The Healing at the Wound.	Left Lobe at Autopsy.	Right Lobe at Autopsy.	Clinical History.	Died.	Autopsy.	Transplantations.	Total Extirpations.
1. (11).	Small dog æt. about 1 year.	17, II, 1888.	* Perforating skin stitches.	Suppuration.			Double keratitis. Died with typical total extirpation symptoms. Suppuration having occurred, this case is of no value as a transplantation experiment.	20, II, 1888.	Negative.	2	1
2. (12).	Medium sized dog.	17, II, 1888.	* Perforating skin stitches.	Absolutely per primam.	Not adherent.	Not adherent.	Died with typical symptoms.	20, II, 1888.	Negative.	2†	1
3. (13).	Medium sized bull dog.	17, II, 1888.	* Perforating skin stitches.	Suppuration.			Died with typical symptoms.	29, II, 1888.		2	1
4. (14).	Small young bitch.	21, II, 1888.	* Perforating skin stitches.	No union; but suppuration not evident.	Not adherent.	Not adherent.		27, II, 1888.	A greyish necrotic film lined the wound. The solution of corros. sublimat. employed for irrigation was probably too strong.	2	1
5. (15).	Large old dog.	21, II, 1888.	* Perforating skin stitches.	No union; but suppuration not evident.	Not adherent.	Not adherent.		24, II, 1888.	Same as preceding case.	2	1

* Antiseptic precautions, closed wound and plaster of Paris dressing. † Healed per primam.

6. (16).	Medium sized dog about one year old.	24, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Necrotic.	Absorbed.	Typical symptoms.	12, III, 1888.	In the neighborhood of right lobe the tissues are stained yellow by material composed of fat globules and needle-shaped fat crystals.	2†	1
7. (18).	Small bitch pup.	24, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Soft yellow necrosed mass.	Necrosed and almost absorbed.	Double conjunctivitis. Typical symptoms.	4, III, 1888.	Very small discrete areas of pneumonia throughout right lung. Other organs healthy.	2†	1
8. (19).	Small young bitch.	27, II, 1888.	* Buried skin stitches.	Wound apparently aseptic.	Not adherent.	Not adherent.		28, II, 1888.	Negative.	2	1
9. (20).	Large dog.	27, II, 1888.	* Buried skin stitches.	Absolutely per primam-	Adherent to surrounding tissues.	Adherent to surrounding tissues.		2, III, 1888.	Negative.	2†	1
10. (21).	Small old dog.	27, II, 1888.	* Buried skin stitches.	Suppuration.	Not adherent and partially absorbed.	Not adherent and partially absorbed.	Convulsions observed only once(4, III).	6, III, 1888.	Double pneumonia.	2	1
11. (23).	Medium sized dog 3 or 4 years old.	28, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Adherent and necrosed.	Adherent and necrosed.	Typical symptoms.	12, III, 1888.	Negative.	2†	1
12. (24).		28, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Adherent and necrosed. Beginning organization new vessels	Adherent and necrosed. Beginning organization.	Typical symptoms.	14, III, 1888.	Negative.	2†	1

*Antiseptic precautions, closed wound and plaster of Paris dressing. † Healed per primam.

TABLE II.—(*Continued.*)

No.	Description of Animal.	Date of Operation.	The Treatment of the Wound.	The Healing of the Wound.	Left Lobe at Autopsy.	Right Lobe at Autopsy.	Clinical History.	Died.	Autopsy.	Transplantations.	Total Extirpations.
13. (25).	Small dog.	28, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Firmly adherent and necrosed.	Firmly adherent and necrosed.	Typical symptoms.	3, III, 1888.	Negative.	2†	1
14. (26).	Small dog about 2 years old.	29, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Not adherent and atrophied.	Firmly adherent and necrosed.	Typical symptoms.	7, III, 1888.	Negative.	2†	1
15. (27).	Medium sized dog about two years old.	29, II, 1888.	* Buried skin stitches.	Wound filled with blood at autopsy.	Not adherent.	Not adherent.	Typical symptoms. Dog killed when moribund to obtain fresh nerve tissues.	6, III, 1888.	Negative.	2	1
16. (28).	Small old bitch.	29, II, 1888.	* Buried skin stitches.	Wound healed in deep parts. Slight suppuration in skin.	Adherent and necrosed.	Adherent and necrosed.	Typical symptoms.	5, III, 1888.	Negative.	2†	1
17. (29).	Medium sized young dog.	29, II, 1888.	* Buried skin stitches.	Absolutely per primam.	Adherent. Color greenish red. Mottled bluish red necrosed. A few preserved follicles at periphery.	Same as left lobe.	Typical symptoms.	12, III, 1888.	Negative.	2†	1
18. (53).	Old bitch.	12, III, 1888.	* Buried skin stitches.	Apparently not infected.				15, III, 1888.	Double pneumonia.	2†	1

*Antiseptic precautions, closed wound and plaster of Paris dressing. †Healed per primam.

19. (54).		12, III, 1888.	* Buried skin stitches.	Absolutely per primam.	Hemorrhagic veins tied first.	Same as left lobe.	Double conjunctivitis. Typical symptoms.	19, III, 1888	Double pneumonia.	2†	1
20. (59).	Large bull dog.	14, III, 1888	* Buried skin stitches.	Absolutely per primam.	Destroyed.	Destroyed.	Lived 62 days. Killed by other dogs and neck devoured. Hence no specimens.	15, V, 1888.	Negative.	2†	1
21. (60).	Small dog about 2 years old.	14, III, 1888.	* Buried skin stitches.	Hemorrhage in wound.			Double conjunctivitis. Typical symptoms.	20, III, 1888.	Negative.	2	1
22. (61).	Large dog about 3 years old.	14, III, 1888.	* Buried skin stitches.	Suppuration.			Typical symptoms.	19, III, 1888.	Fetid pleurisy by extension from neck wound.	2	1
23. (62).	Large old dog.	15, III, 1888.	* Buried skin stitches.	Suppuration.			Conjunctivitis of left eye. Symptoms of total extirpation	21, III, 1888.	Negative.	2	1
24. (65).	Small young dog.	15, III, 1888.	* Buried skin stitches.	Absolutely per primam.			Symptoms of total extirpation. When almost dead was bled to death in a transfusion experiment.	20, III, 1888.	Negative.	2†	1
										22 26†	
										48	24

* Antiseptic precautions, closed wound and plaster of Paris dressing. † Healed per primam.

TABLE III.—*Piecemeal Resection of the Thyroid Gland.*

No.	Description of animal.	Resected at 1st operation.	Examination of piece resected at 1st op.	Resected at 2nd operation.	Examination of pieces resected at 2nd op.	Resected at 3rd operation.	Examination of piece resected at 3rd op.	Resected at 4th operation.	Examination of piece resected at 4th op.	Resected at 5th operation.	Examination of piece resected at 5th op.	Died or killed.	Examination of accessory thyroids and final piece.	Remarks.
1. (81).	Dog, æt. about 1 year.	4, X, 1888. Inf. ⅓ left lobe.	Normal.	23, XI, 1888. Sup. ⅓ left. Inf. ½ right.	50 days after 1st op. Left, 0·7 grm., hypertrophied. Right, 1·75 (estimate), hypertrophied.	30, IV, 1889. Middle ½ right.	158 days after 2nd op. 208 days after 1st op. 1 grm. Hypertrophied.	9, VIII, 1889. Inf. ⅓ of sup. or remaining ⅓ of right.	101 days after 3rd op. 309 days after 1st op. Hypertrophied.			24, VIII, 1889. Strangled by piece of meat lodged in pharynx.	324 days after 1st op. Suprasternal and aortic enlarged and hypertrophied.	
2. (82).	Bitch, æt. about 1 year.	13, X, 1888. Inf. ⅔ of left lobe.	Wt. 0·6 (estimate). Normal.									6, I, 1889. Pneumonia.	85 days after op. Left, wt. 1·5, hypertrophied. Right, wt. 2·7, hypertrophied.	
3. (83).	Old dog.	13, X, 1888. Inf. ⅓ left.	Wt. 0·4 (estimate). Normal.	5, XII, 1888. Sup. ⅓ left. Inf. ⅔ right.	53 days after 1st op. Left hypertrophied. Right hypertrophied.							22, XII, 1889. Strangled by piece of meat lodged in pharynx.	70 days after 1st op. Sup. ⅔ right. Hypertrophied.	
4. (84).	Dog, æt. about 1 year.	17, X, 1888. Inf. ⅓ left.	Normal.									7, I, 1889. Killed to make injection of right lobe.	82 days after op. Sup. ⅓ left, large and hypertrophied. Right, large and hypertrophied.	
5. (85).	Small old bitch.	17, X, 1888. Inf. ⅓ left.	Wt. 0·25. Normal.	29, I, 1889. Sup. ⅓ left. Inf. ⅔ right.	104 days after 1st op. Moderate hypertrophy. Colloid still in many follicles. Fig. 7.							8, II, 1889. Killed by other dogs.	Destroyed by dogs.	
6. (86).	Medium sized dog, æt. about 2 years.	23, X, 1888. Inf. ⅓ left.	Wt. 0·6. Normal.	12, XII, 1888. Sup. ⅓ left. Inf. ⅓ right.	50 days after 1st op. Left, wt. 2. (est.), hypertrophied. Right, wt. 1. (est.), hypertrophied.	12, II, 1889. Inf. ⅓ of remainder of right (2nd, 4th).	62 days after 2nd op. 112 days after 1st op. Hypertrophied.	28, IV, 1889. Inf. ⅓ of rest of right (2nd, 8th).	75 days after 3rd op. 187 days after 1st op. Hypertrophied.			19, V, 1889. Symptoms character of thyroid extirpation.	Several unusual accessory thyroids. Vid. history. All hypertrophied.	Lived 21 days with only ⅛ of both lobes.

7. (87).	Medium sized full grown dog.	23, X, 1888. Inf. ⅓ left.	Wt. 0.3. Normal.	11, XII, 1888. Sup. ⅓ left. Inf. ⅓ right.	49 days after 1st op. Left, moderate hypertrophy. Right, moderate hypertrophy.							17, XII, 1888. Killed when dying.	Remainder of right lobe had sloughed.
8. (88).	Small young bitch.	23, X, 1888. Inf. ⅓ left.	Wt. 0.25. Normal.									7, XI, 1888. Killed to make injected specimens.	15 days after op. Sup. ⅓ left, hypertrophy well marked. Right, hypertrophy well marked.
9. (89).	Small bitch, æt. about 1 yr.	26, X, 1888. Inf. ⅓ left.	Wt. 0.4. Normal.									3, I, 1889. Pneumonia.	
10. (90).	Large strong dog æt. 2 or 3 years.	26, X, 1888. Inf. ⅓ left.	Wt. 0.3. Normal.	29, I, 1889. Sup. ⅓ left. Inf. ⅓ right.	95 days after 1st op. Left hypertrophied. Right hypertrophied.	30, IV, 1889. Inf. ⅓ of remainder right.	91 days after 2d op. 186 days after 1st op. Wt. 1 5. Hypertrophied.					21, VI, 1889. Probably too little thyroid.	238 days after 1st op. Wt. of rest of right, 2. Hypertrophied.
11. (91).	Large dog æt. 2 or 3 years.	26, X, 1888. Inf. ⅓ left.	Wt. 0.8. Normal.									5, I, 1889. Pneumonia.	71 days after 1st op. Follicles of remaining pieces filled with cells. No hypertrophy.
12. (92).	Small puppy dog æt. about 6 mos.	31, X, 1888. Inf. ⅓ left.	Wt. 0.3. Normal.	12, XII, 1888. Sup. ⅓ left. Inf. ⅓ right.	42 days after 1st op. Left and right normal.							17, XII, 1888. No definite symptoms of thyroid extirpation.	Autopsy 2 days after death. Accessories and final piece decomposed.
13. (93.)	Bitch, æt. about 3 years.	31, X, 1888. Inf. ⅓ left.	Normal.									26, XI, 1888. Purulent pericarditis and pleuritis.	26 days after op. Early hypertrophy.
14. (94).	Small young dog.	31, X, 1888. Inf. ⅓ left.	Normal.									7, II, 1889. Killed to make injected specimens.	99 days after op. Left and right hypertrophied.
15. (95).	Small puppy dog.	2, XI, 1888. Inf. ⅓ left.	Normal.									Dog lost.	
16. (96).		2, XI, 1888. Sup. ½ left.										4, I, 1889. Pneumonia.	63 days after op. Left, wt. 1.8, hypertrophied. Right, wt. 3.6, hypertrophied.

TABLE III.—(*Continued.*)

No.	Description of animal.	Resected at 1st operation.	Examination of piece resected at 1st op.	Resected at 2nd operation.	Examination of pieces resected at 2nd op.	Resected at 3rd operation.	Examination of piece resected at 3rd op.	Resected at 4th operation.	Examination of piece resected at 4th op.	Resected at 5th operation.	Examination of piece resected at 5th op.	Died or killed.	Examination of accessory thyroids and final piece.	Remarks.
17. (97).	Small bitch, æt. about 1 year.	14, XI, 1888. Sup. ½ left.	Normal.	12, XII, 1888. Intended to resect rest of left, but could find nothing but ligature of 1st op.		30, IV, 1889. Inf. ½ right.	139 days after 2nd op. 167 days after 1st op. Very large, spindle shaped. Hypertrophied.	11, XI, 1889. ½ of lymph gland by mistake.	195 days after 3rd op. 362 days after 1st op. Lymph gland.	6, I, 1890. Remainder of right after prolonged search.	56 days after 4th op. 418 days after 1st op. Small hard nodule. Hypertrophied.	14, I, 1890. With symptoms typical of thyroid extirpation.	426 days after 1st op. Accessories hypertrophied.	12, IV, 1889, bitch at full term. Convulsions yesterday and to-day, otherwise well and in good spirits. 13, IV, 1889, whelped five pups with tremendous thyroids. Vid. full history and 20 (127).
18. (98).														
19. (126).	Small bitch, æt. about 2 years.	11, XII, 1888. Ligation of left lobe about 2 mm. above inf. pole.	Nothing resected.	22, IV, 1889. Entire left and inf. ⅔ right.	132 days after 1st op. Left, normal. (?) Right, early hypertrophy.	9, VIII, 1889. Inf. ½ of remaining ⅔ of right.	109 days after 2nd op. 241 days after 1st op. Hypertrophy.	11, XI, 1889. Remainder (sup. $\frac{2}{3}$) of right.	93 days after 3rd op. 334 days after 1st op. Hypertrophied.			11, XI, 1889. Killed by morphia at 4th op. Had been very weak for several weeks and would soon have died.	334 days after 1st op. Accessories hypertrophied.	
20. (127).	Medium sized pointer bitch, about 1 year old.	11, XII, 1888. Ligation of left lobe about 3 mm. above inf. pole.	Nothing resected.	22, IV, 1889. Entire left and inf. ½ right.	132 days after 1st op. Normal.	11, XI, 1889. Middle ½ right.	203 days after 2nd op. 335 days after 1st op. Nearly normal.	14, I, 1890. Inf. ⅔ of remaining sup. ½ of right, (2nd and 3rd ninths.)	64 days after 3rd op. 339 days after 1st op. Wt. 1.5. (⅔ of right). Hypertrophied.	Jan., 1891. Remainder (sup ⅓) of right. Lived 1 year with $\frac{1}{10}$ of both lobes.	2 years and 1 mo. after 1st op. Specimen lost.	Jan., 1891. 3 or 4 days after 5th op. With typical symptoms of thyroid extirpation.	2 years and 1 mo. after 1st op. Accessories hypertrophied.	31, VIII, 1889. Has had convulsions and typical symptoms of thyroid extirpation for 2 days. Previously was quite well. Whelped 8 pups. Vid. No. 17, (97), and full history. Lived 1 year with $\frac{1}{10}$ of both lobes.

TABLE IV:—*Condition of Undisturbed (Right) Lobe after Extirpation of or Various Insults to the other (Left) Lobe.*

No. of dog.	Operation.	From first operation to removal of right lobe.	Condition of right lobe.	
(1.) 116.	Extirpation of left lobe. Open treatment of wound.	3 hours.	Normal.	
(2.) 110.	Extirp. l. lobe. Open treatment of wound.	28 hours.	Normal.	
(3.) 118.	Extirp. l. lobe. Open treatment of wound.	4 days.	Normal.	
(4.) 120.	Extirp. l. lobe. Open treatment of wound.	7 days.	Epithelium of right lobe higher than that of left lobe.	Slight changes in shape of follicles of right lobe.
(5) 121.	Extirp. l. lobe. Open treatment of wound.	7 days.	Normal.	
(6.) 108.	Extirp. l. lobe. Open treatment of wound.	10 days.	Epithelium of right lobe somewhat higher than that of left lobe.	Epithelium of left lobe a little higher than normal.
(7.) 119.	Extirp. l. lobe. Open treatment of wound.	10 days.	Normal.	
(8.) 124.	Extirp. l. lobe. Open treatment of wound.	13 days.	Normal.	
(9.) 58.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*15 days.	Hypertrophy. High epithelium, angular follicles. Colloid absent. No involutions. Right lobe obtained post mortem.	Capillary buds not covered by epithelium project into follicles of right lobe. Extensive hemorrhages into left (necrotic) lobe. No tremors nor convulsions. Lungs normal. Scorbutic gums.
(10.) 88.	Extirp. inf. half l. lobe. Open treatment of wound.	15 days.	Hypertrophy quite advanced. Involutions.	
(11.) 79.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	17 days.	Normal, except that many of the follicles are filled with cells. Right lobe obtained post mortem, was white and hard.	No convulsions nor tremors. Autopsy negative.

* Died.

TABLE IV.—(*Continued.*)

No. of dog.	Operation.	From first operation to removal of right lobe.	Condition of right lobe.	
(12.) 125.	Ligation of everything at upper poles except the arteries. Open treatment of wound.	17 days.	Hypertrophy, early stage.	
(13.) 64.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*18 days.	Normal, except that follicles are filled with cells. Right lobe obtained post mortem.	Scorbutic gingivitis. No convulsions nor tremors. Autopsy negative.
(14.) 76.	Extirp. l. lobe and substitution transplantation. Closed wound. Plaster of Paris dressing. Healed per primam.	*18 days.	Normal. Follicles for the greater part filled with cells. Right lobe obtained post mortem.	Scorbutic gingivitis. No convulsions nor tremors. Autopsy negative.
(15.) 122.	Extirp. right lobe. Open treatment of wound.	19 days.	Normal.	
(16.) 123.	Extirp. l. lobe. Open treatment of wound.	19 days.	Epithelium slightly higher in right than in left lobe. Follicles more angular and colloid thinner.	
(17.) 66.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*20 days.	Epithelium abnormally high in places. Many follicles filled with cells. Right lobe obtained post mortem.	Dog died of pneumonia on 20th day after operation.
(18.) 50.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*20 days.	Normal. Some follicles filled with cells. Right lobe obtained post mortem.	No convulsions nor tremors. Autopsy negative.
(19.) 75.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*20 days.	Follicles filled with cells. Epithelium in one of three sections higher than normal. Right lobe obtained post mortem.	No convulsions nor tremors. Gums normal. Autopsy negative.
(20.) 112.	Extirp. l. lobe. Open treatment of wound.	22 days.	Normal.	
(21.) 35.	Manipulation enucleation. Vessels uninjured. Closed wound. Plaster of Paris dressing. Healed per primam.	*24 days.	Cuboidal epithelium. Many follicles filled with these high cells. Colloid absent. No involutions. Right lobe obtained post mortem.	Pneumonia of right lung.

* Died.

(22.)	68.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*25 days.	Epithelium higher than in left lobe. Colloid disappeared. Follicles slightly angular. No involutions. Right lobe obtained post mortem.	Gangrene of gums and sides of tongue. Gangrenous ulcer on dorsum of tongue. Small pneumonic area in left lung.
(23.)	93.	Extirp. inf. half l. lobe. Open treatment of wound.	26 days.	Early hypertrophy.	
(24.)	72.	Extirp. l. lobe and substitution transplantation. Closed wound. Plaster of Paris dressing. Healed per primam.	*39 days.	No hypertrophy. Most follicles filled with cells. Right lobe obtained post mortem.	No convulsions nor tremors. Extensive scorbutic gingivitis. Lungs normal.
(25.)	92.	Extirp. inf. half l. lobe. Open treatment of wound.	42 days.	Inferior half right lobe very early stage of hypertrophy. High epithelium. Colloid present.	Follicles filled with cells in sup. ½ of right lobe (removed at autopsy).
(26.)	109.	Complete extirp. l. lobe. Open treatment of wound.	45 days.	Early hypertrophy. High epithelium. Thin colloid. Angular follicles. No involutions.	
(27.)	87.	Extirp. inf. half l. lobe. Open treatment of wound.	49 days.	Hypertrophy. Very high epithelium. No colloid. Angular follicles and involutions.	
(28.)	81.	Extirp. inf. half l. lobe. Open treatment of wound.	50 days.	Advanced hypertrophy.	
(29.)	86.	Extirp. inf. half l. lobe. Open treatment of wound.	50 days.	Advanced hypertrophy.	
(30.)	105.	Ligation of everything at upper poles except arteries. Open treatment of wound.	51 days.	Normal.	No unnecessary manipulations of the lobes during the operation.
(31.)	83.	Extirp. inf. half l. lobe. Open treatment of wound.	53 days.	Hypertrophy. Involutions unusually numerous.	
(32.)	77.	Extirp. l. lobe and substitution transplantation. Closed wound. Plaster of Paris dressing. Healed per primam.	56 days.	Advanced hypertrophy. Dog perfectly well when right lobe was removed.	

* Died.

TABLE IV.—(*Continued.*)

No. of dog.	Operation.	From first operation to removal of right lobe.	Condition of right lobe.	
(33.) 103.	Extracaps. enucleat. both lobes. Principal arts. and veins intact. Open treatment of wound.	*57 days.	Advanced hypertrophy. Weight of left lobe 3 grms. Weight of right lobe 1 grm.	Interesting case because symptoms of total extirpation appeared and disappeared, and because the dog died with symptoms of thyroid privation, notwithstanding the tremendous and hypertrophied lobes.
(34.) 67.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	61 days.	Almost normal. Epithelium slightly higher than normal.	Dog much emaciated when right lobe was removed. Has not been well since first operation.
(35.) 96.	Extirp. sup. ½ left lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	63 days.	Advanced hypertrophy.	
(36.) 69.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Superficial suppuration of wound.	64 days.	Advanced hypertrophy.	Scorbutic gums and loss of hair after first operation. Entire recovery before second operation. Two small gl. parathyroid. found outside of capsule of right lobe. Precisely same structure as right lobe.
(37.) 56.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	*65 days.	Early hypertrophy. Right lobe obtained post mortem.	Scorbutic gums. Central corneal ulcer of left eye. Extensive loss of hair. Had tremors of tongue after first operation, which disappeared in a few days.
(38.) 43.	Extirp. l. lobe and substitution transplantation. Plaster of Paris dressing. Healed per primam.	67 days.	Hypertrophy.	Dog lively and well after first operation. No loss of hair nor inflammation of eyes nor gums.
(39.) 70.	Complete isolation right lobe. Closed wound. Healed per primam.	68 days.	Left lobe hypertrophied. Exceptional case in that right lobe was first operated upon.	Dog had scorbutic gingivitis and lost his hair after first operation, but was perfectly well when left lobe was removed.
(40.) 55.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Healed per primam.	70 days.	Advanced hypertrophy.	Dog well at second operation. There are four intracapsular glandulæ parathyroideæ which have precisely the same structure as the hypertrophied right lobe.

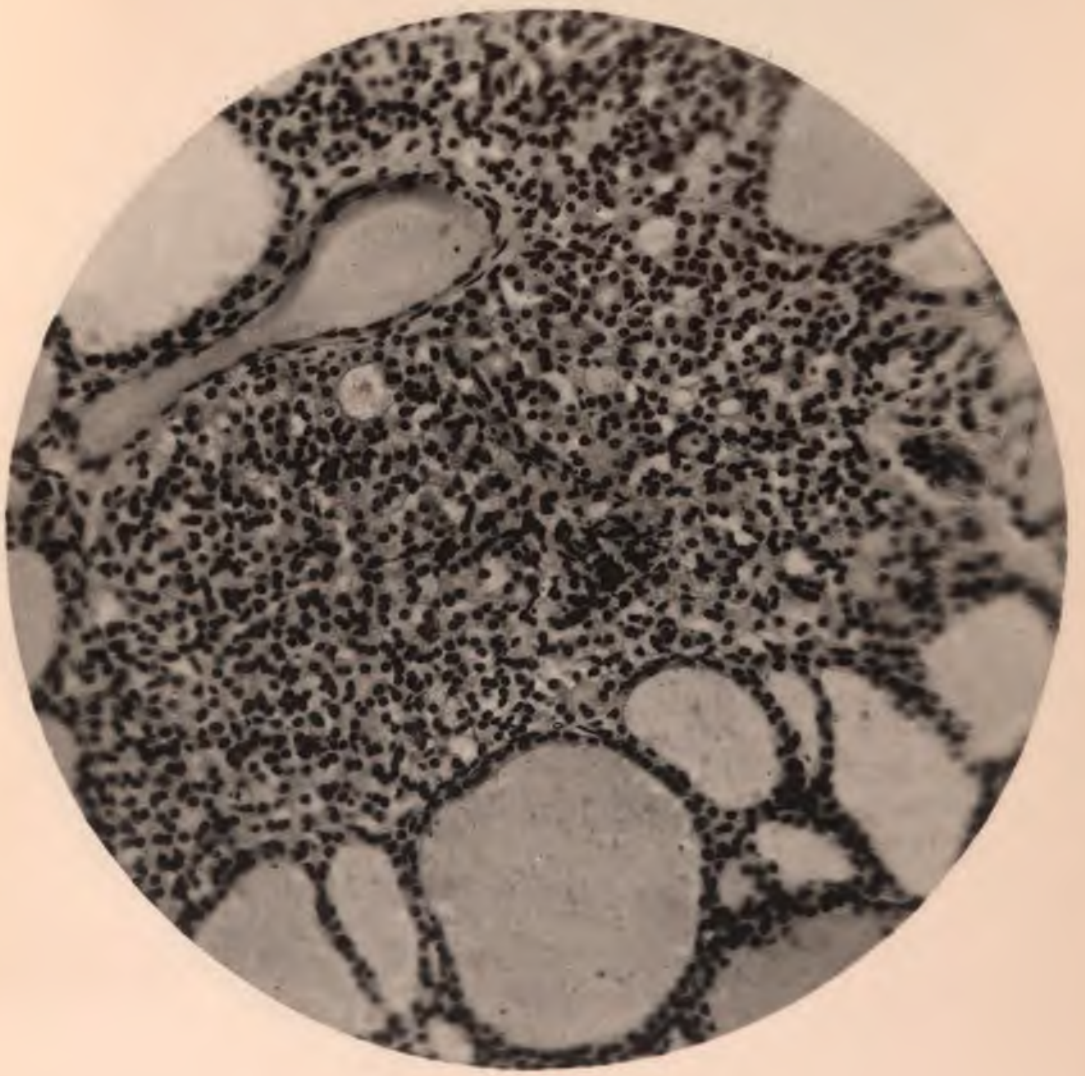
* Died.

(41.)	2.	Extirp. l. lobe. Closed wound. Plaster of Paris dressing. Superficial suppuration at upper angle of wound.	71 days.	Advanced hypertrophy. Weight 2½ grams.	Dog was lively and well until right lobe was removed.
(42.)	91.	Extirp. inf. ⅔ l. lobe. Open treatment of wound.	71 days.	Advanced hypertrophy.	
(43.)	48.	Complete isolation l. lobe. Closed wound. Plaster of Paris dressing. Wound suppurated.	75 days.	Hypertrophy. Festoon stage. Weight 2½ grams.	Dog was apparently well, but quite thin when right lobe was removed.
(44.)	104.	Extracaps. enucleation both lobes. Arts. and veins intact. Open treatment of wound.	82 days.	Hypertrophy. Festoon stage.	Full history given in the text.
(45.)	84.	Extirp. inf. ½ l. lobe. Open treatment of wound.	82 days.	Advanced hypertrophy.	
(46.)	82.	Extirp. inf. ⅔ l. lobe. Open treatment of wound.	85 days.	Advanced hypertrophy.	
(47.)	90.	Extirp. inf. half l. lobe. Open treatment of wound.	95 days.	Advanced hypertrophy.	
(48.)	94.	Extirp. inf. half l. lobe. Open treatment of wound.	99 days.	Advanced hypertrophy.	
(49.)	85.	Extirp. inf. ½ l. lobe. Open treatment of wound.	104 days.	Advanced hypertrophy.	
(50.)	126.	Ligation of l. lobe just above inf. tip. Open treatment of wound.	132 days.	Advanced hypertrophy.	
(51.)	127.	Ligation l. lobe just above inf. tip. Open treatment of wound. 2nd operation. Excised left lobe and inf. ¼ right lobe. 3rd operation. Excised middle ¼ of right lobe.	132 days. 203 days after 2nd operation and 335 days after 1st operation.	Normal. Left lobe and inf. ¼ of right lobe. Early hypertrophy (middle ¼ of right lobe). Colloid present. Epithelium higher than left lobe. Some festooning.	

PHOTOGRAPH I.

40 diameters

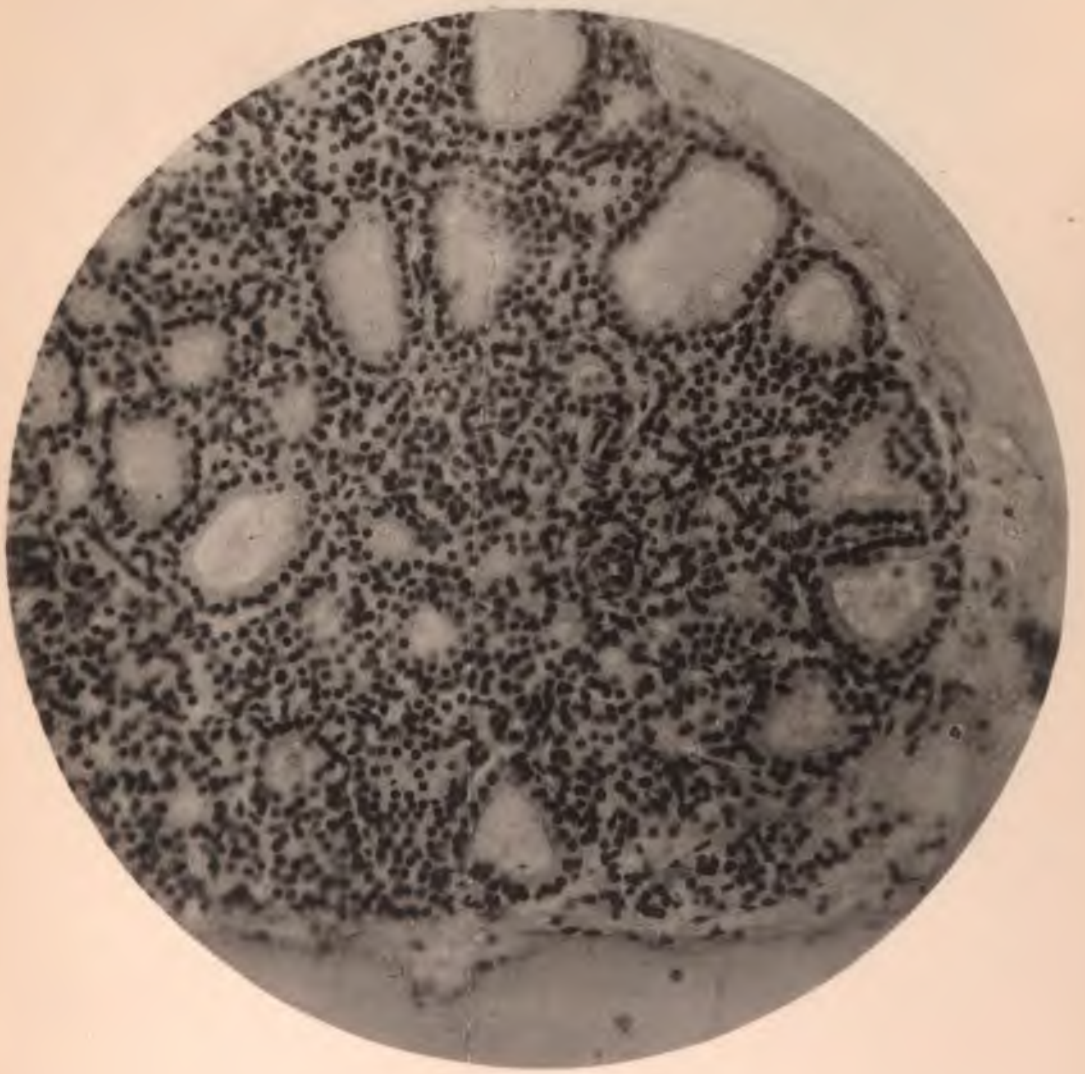
THE HELIOTYPE PRINTING CO., BOSTON.



PHOTOGRAPH II.

275 diameters.

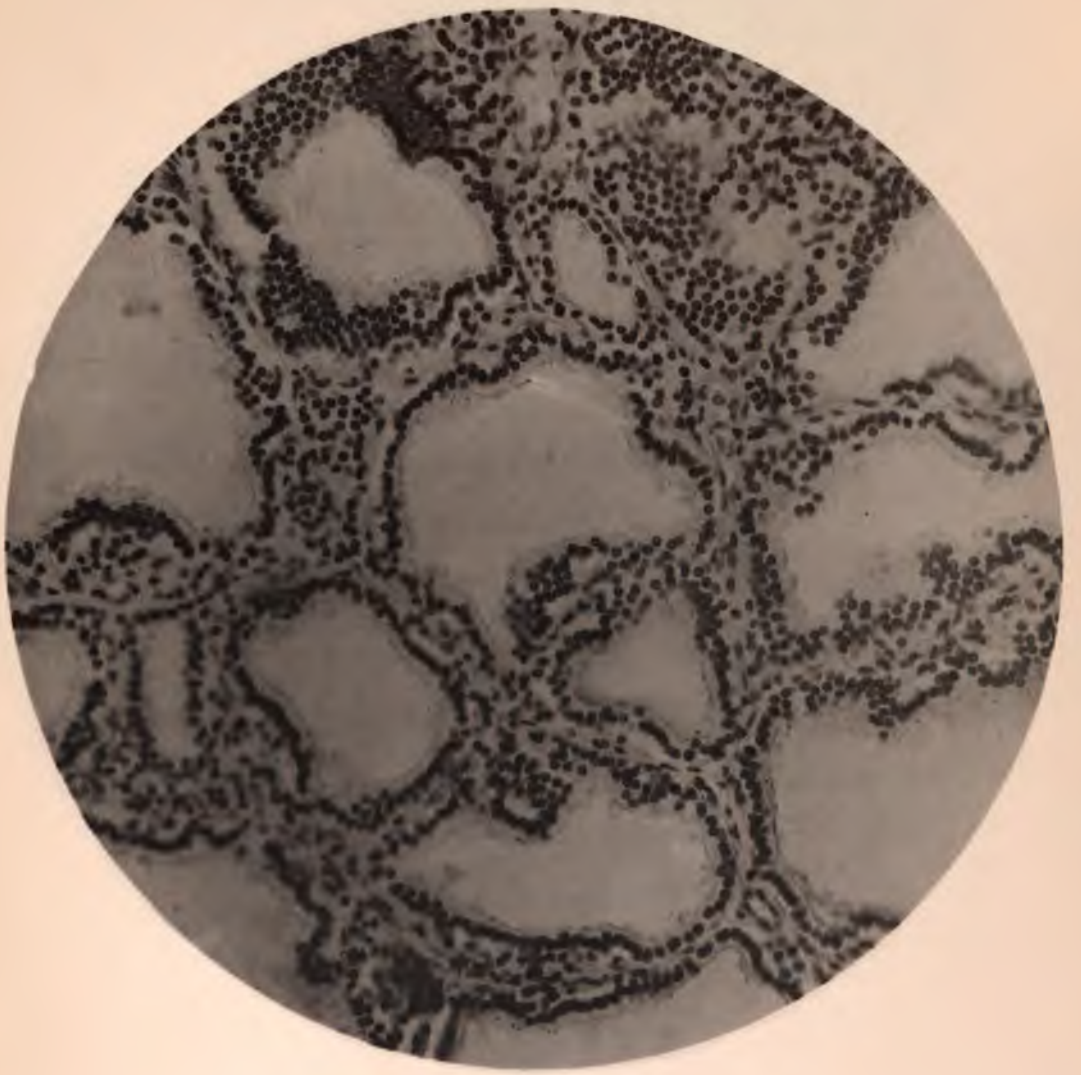
THE HELIOTYPE PRINTING CO., BOSTON



PHOTOGRAPH III.

275 diameters.

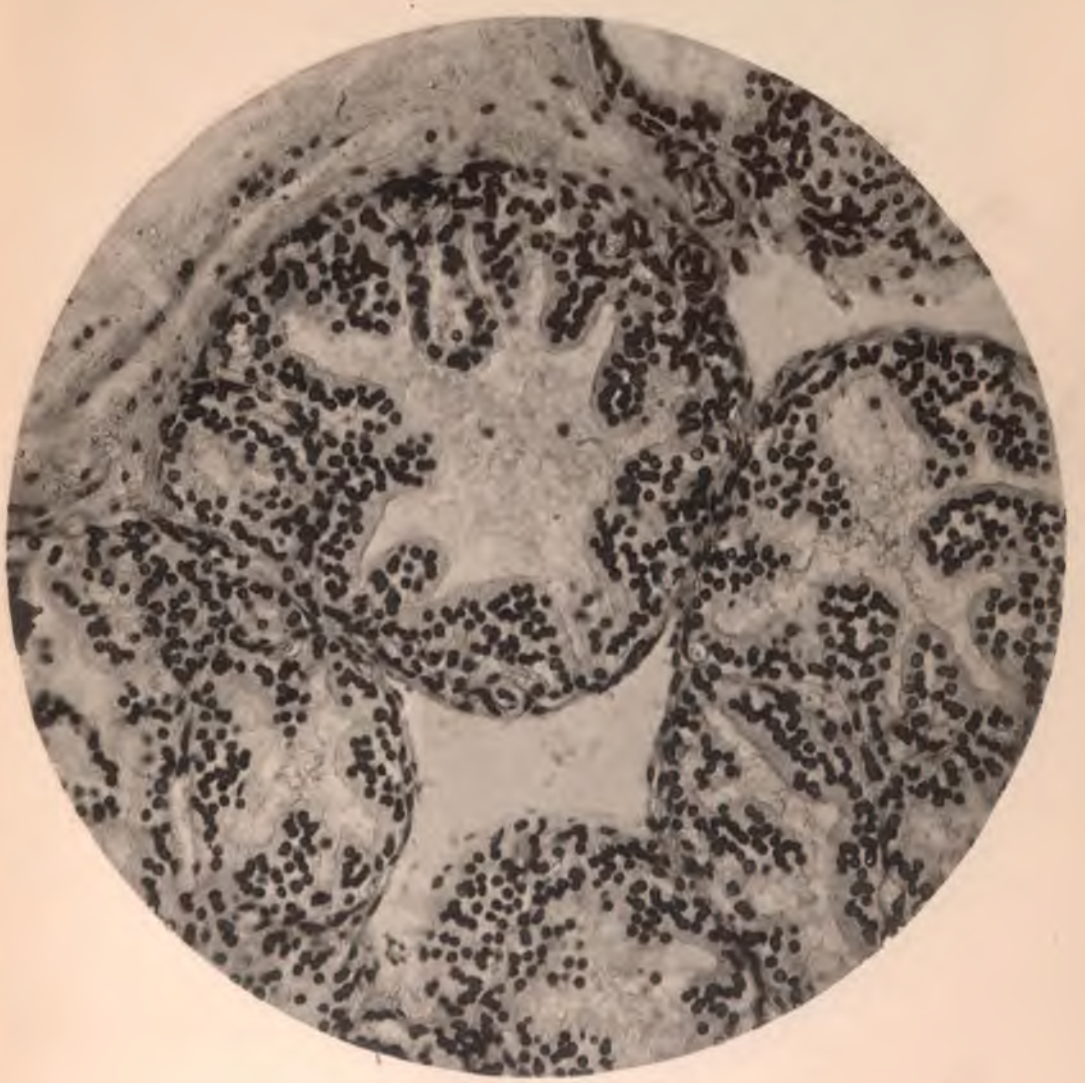
THE HELIOTYPE PRINTING CO., BOSTON.



PHOTOGRAPH IV.

275 diameters.

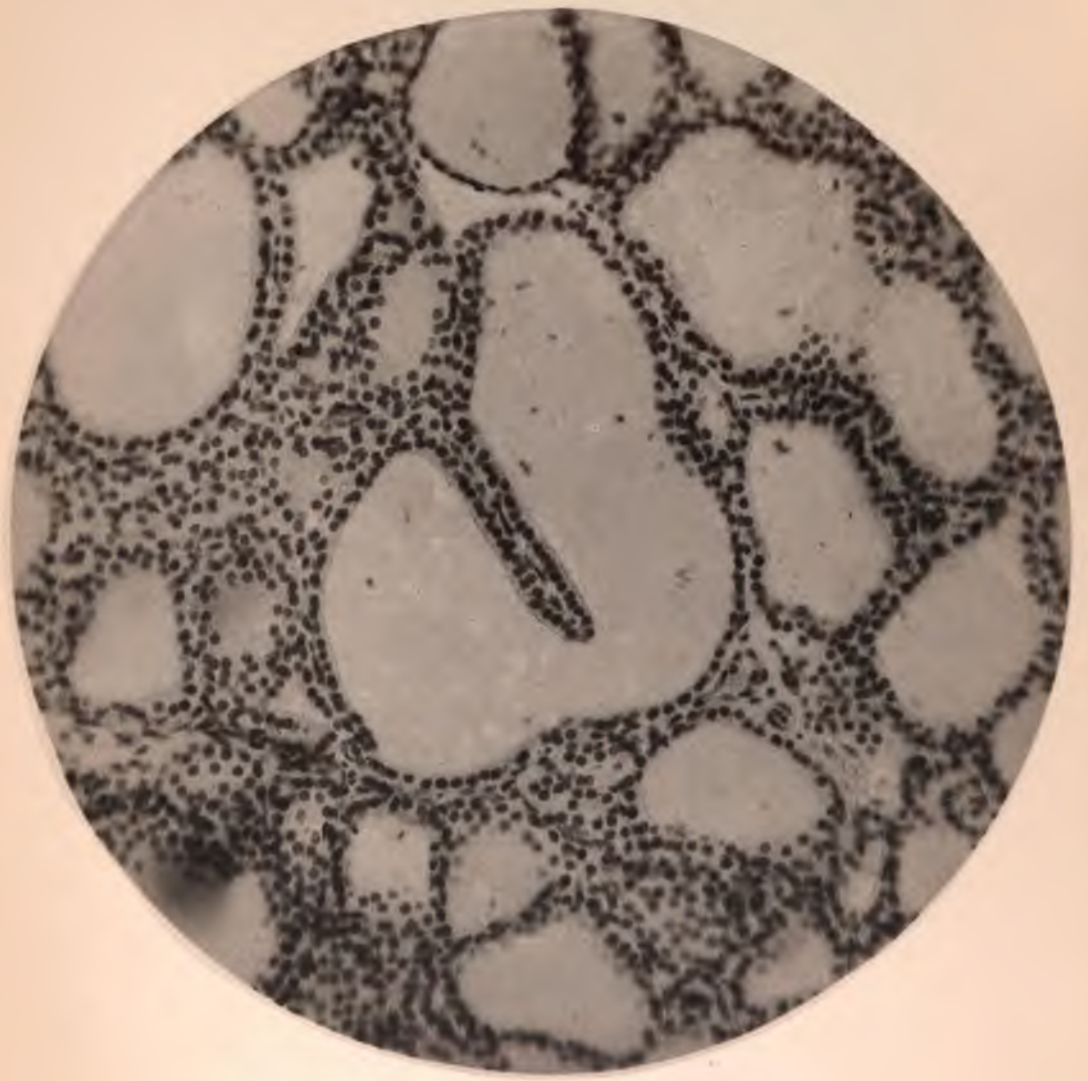
THE HELIOTYPE PRINTING CO., BOSTON



PHOTOGRAPH V.

275 diameters.

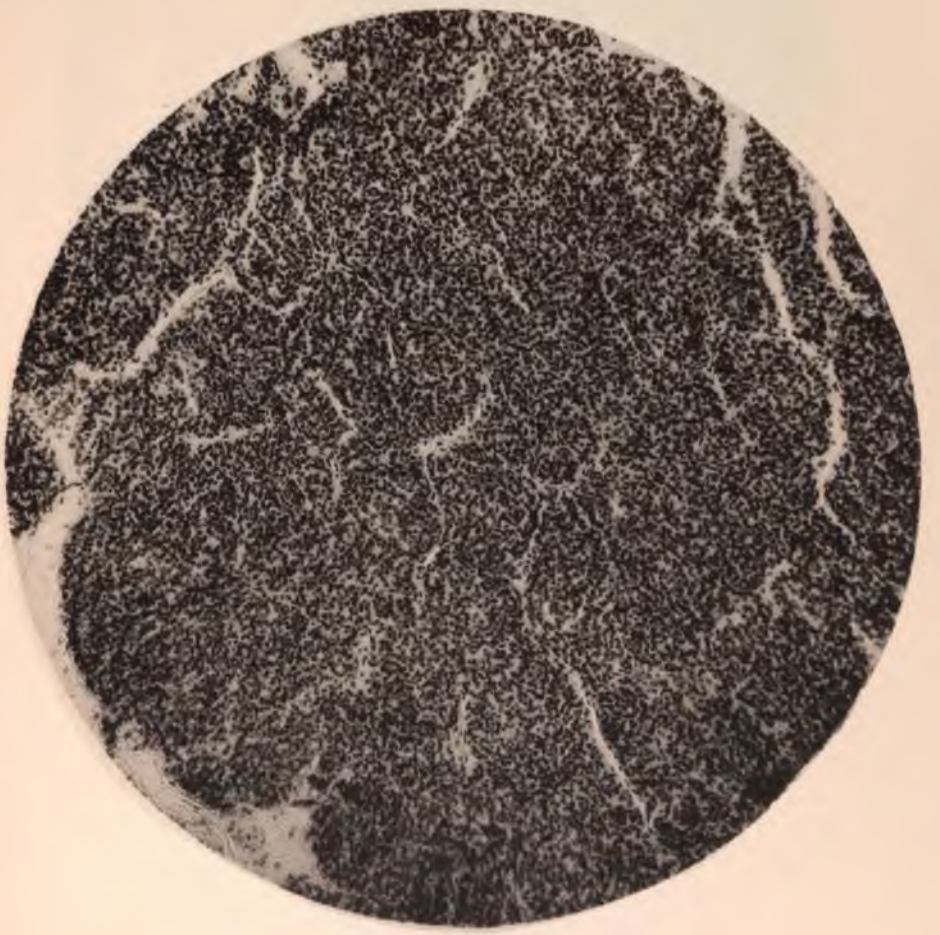
THE HELIOTYPE PRINTING CO., BOSTON.



PHOTOGRAPH VI.

275 diameters.

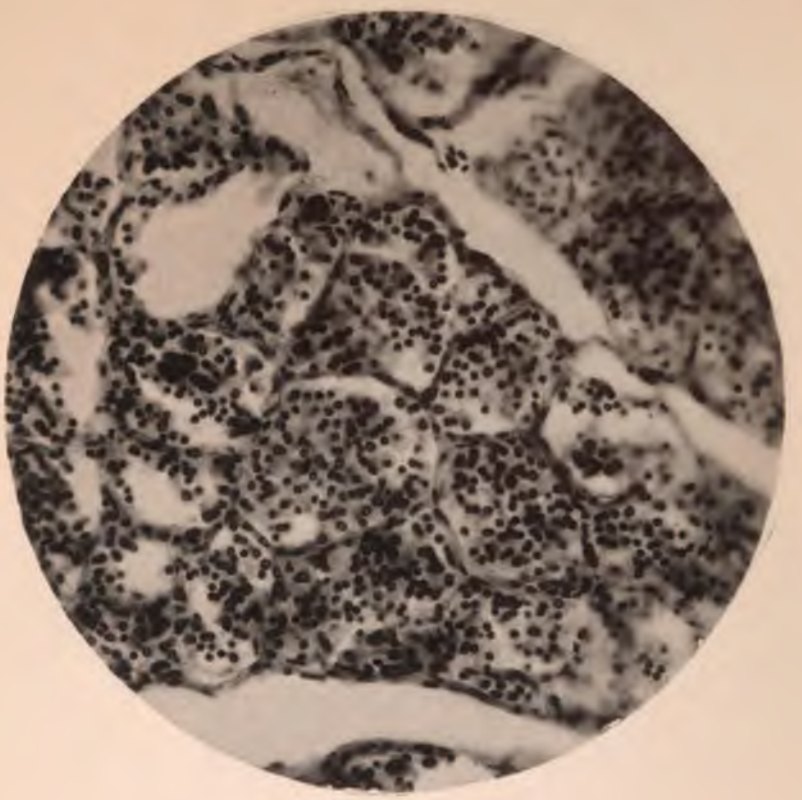
THE HELIOTYPE PRINTING CO., BOSTON



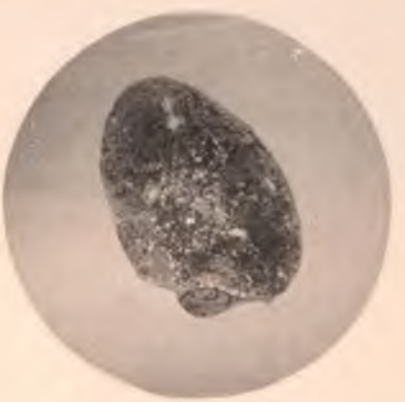
PHOTOGRAPH VII.

68 diameters.

THE HELIOTYPE PRINTING CO., BOSTON.



PHOTOGRAPH VIII.
275 diameters.



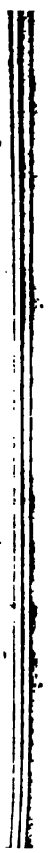
PHOTOGRAPH IX.
12 diameters.

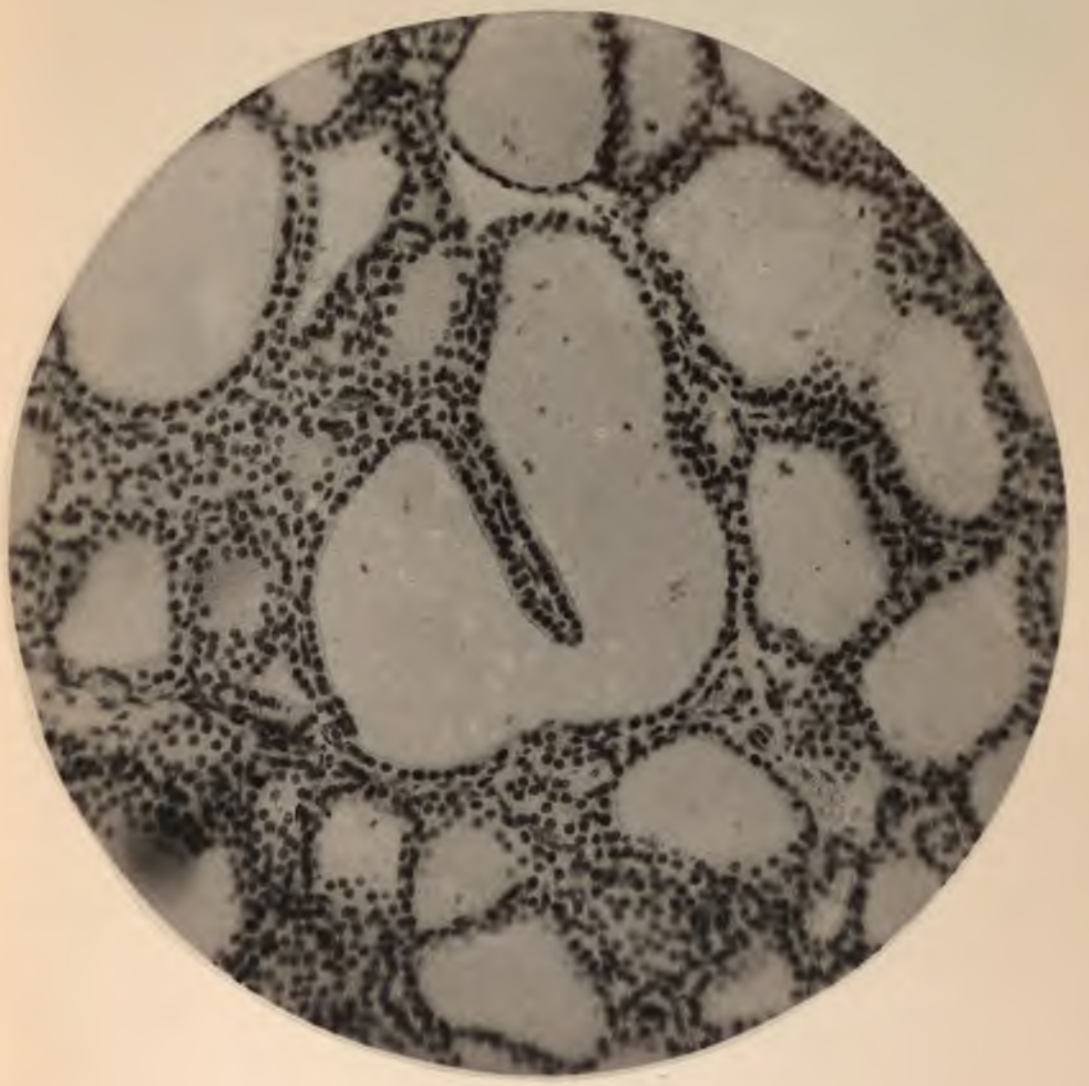
THE HELIOTYPE PRINTING CO., BOSTON

PHOTOGRAPH X.

12 diameters.

THE HELIOTYPE PRINTING CO., BOSTON.

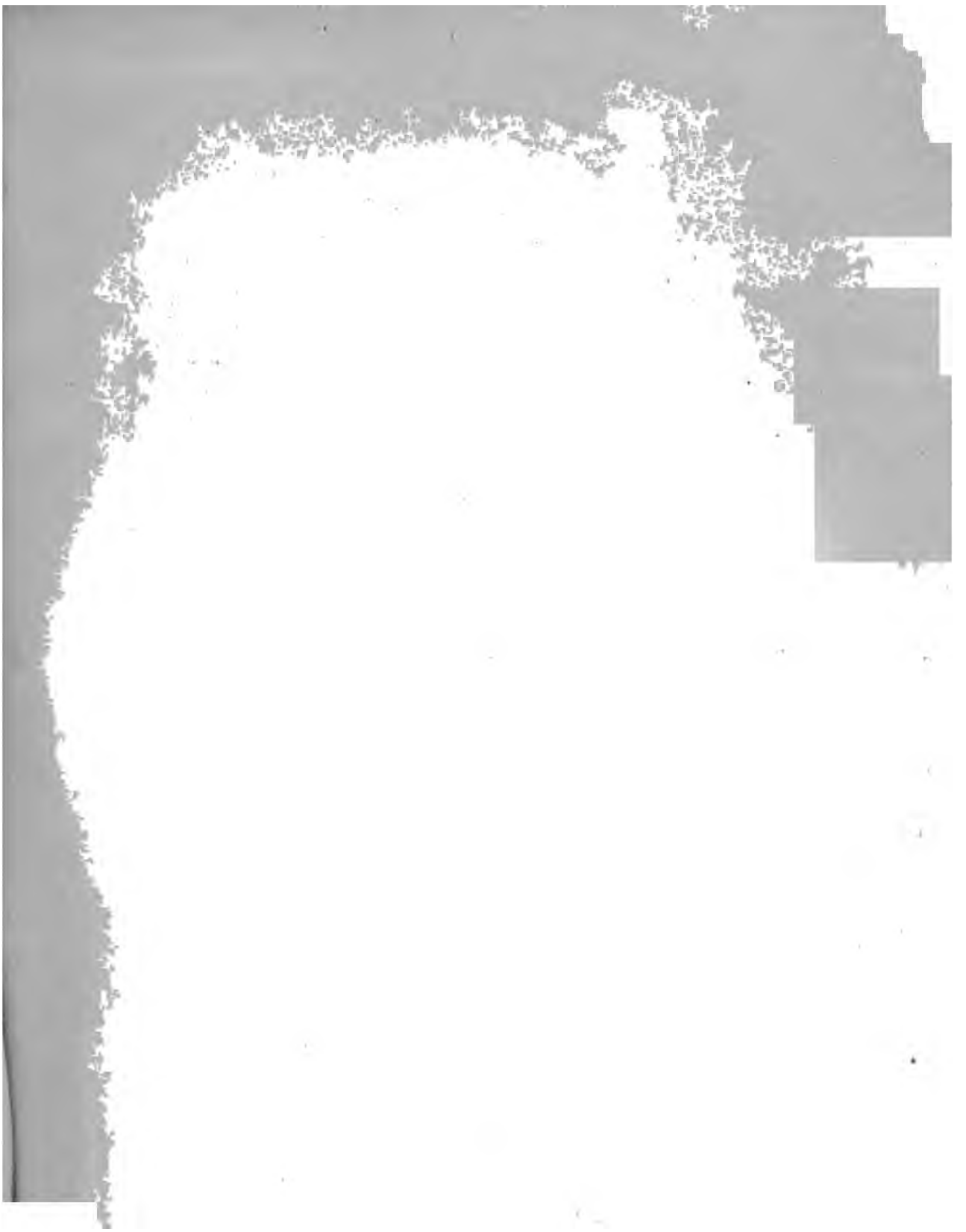


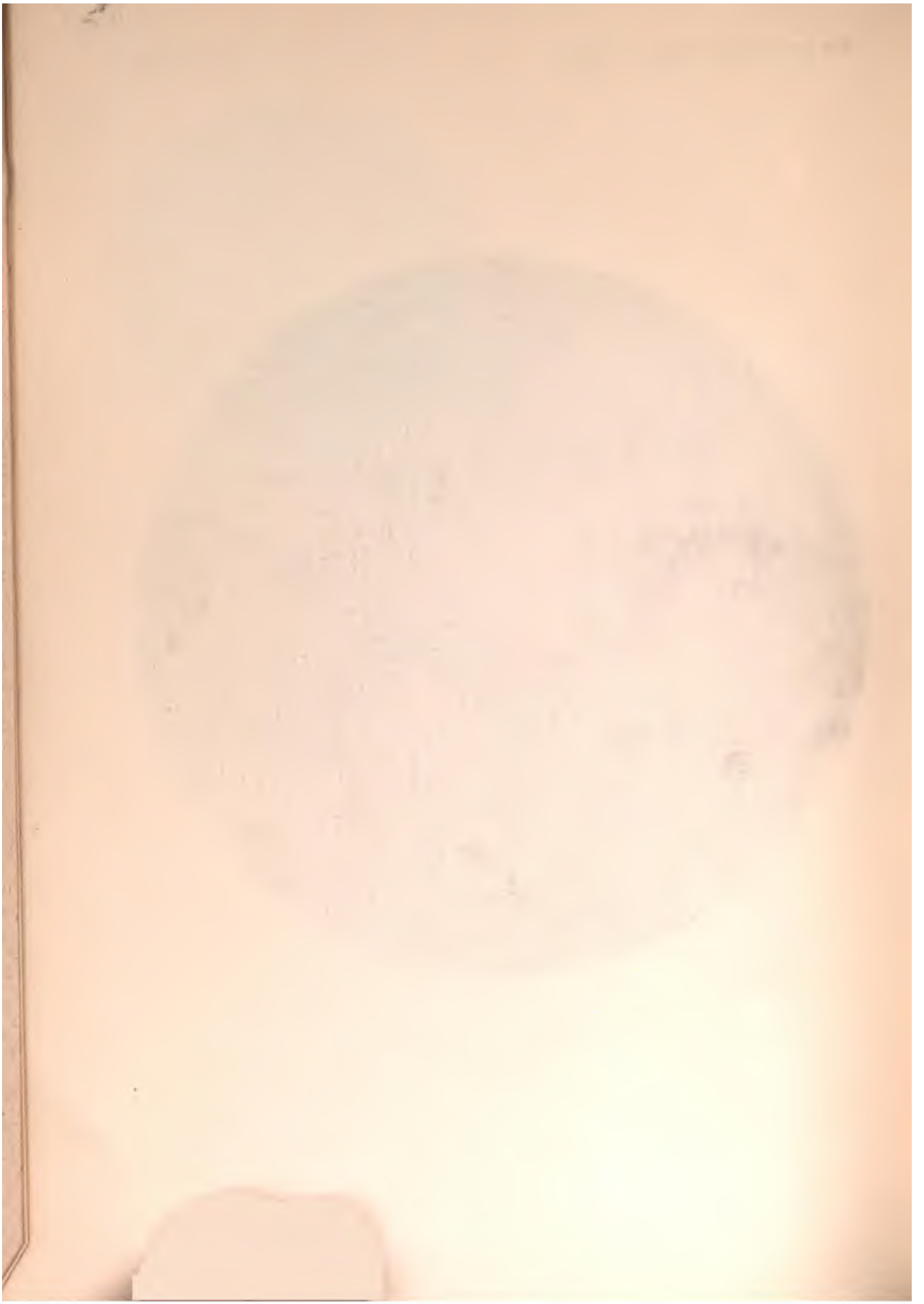


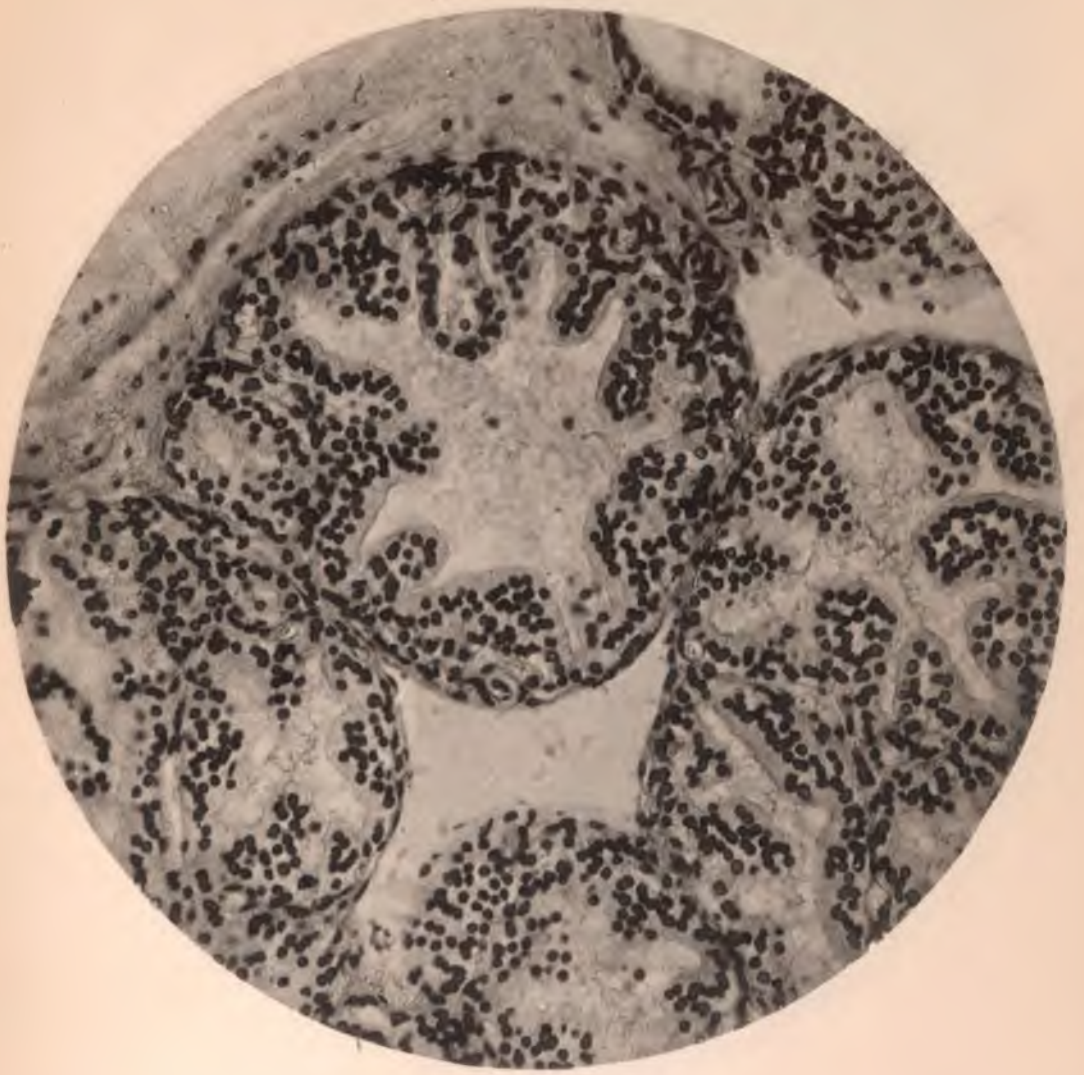
PHOTOGRAPH VI.

275 diameters.

THE HELIOTYPE PRINTING CO., BOSTON



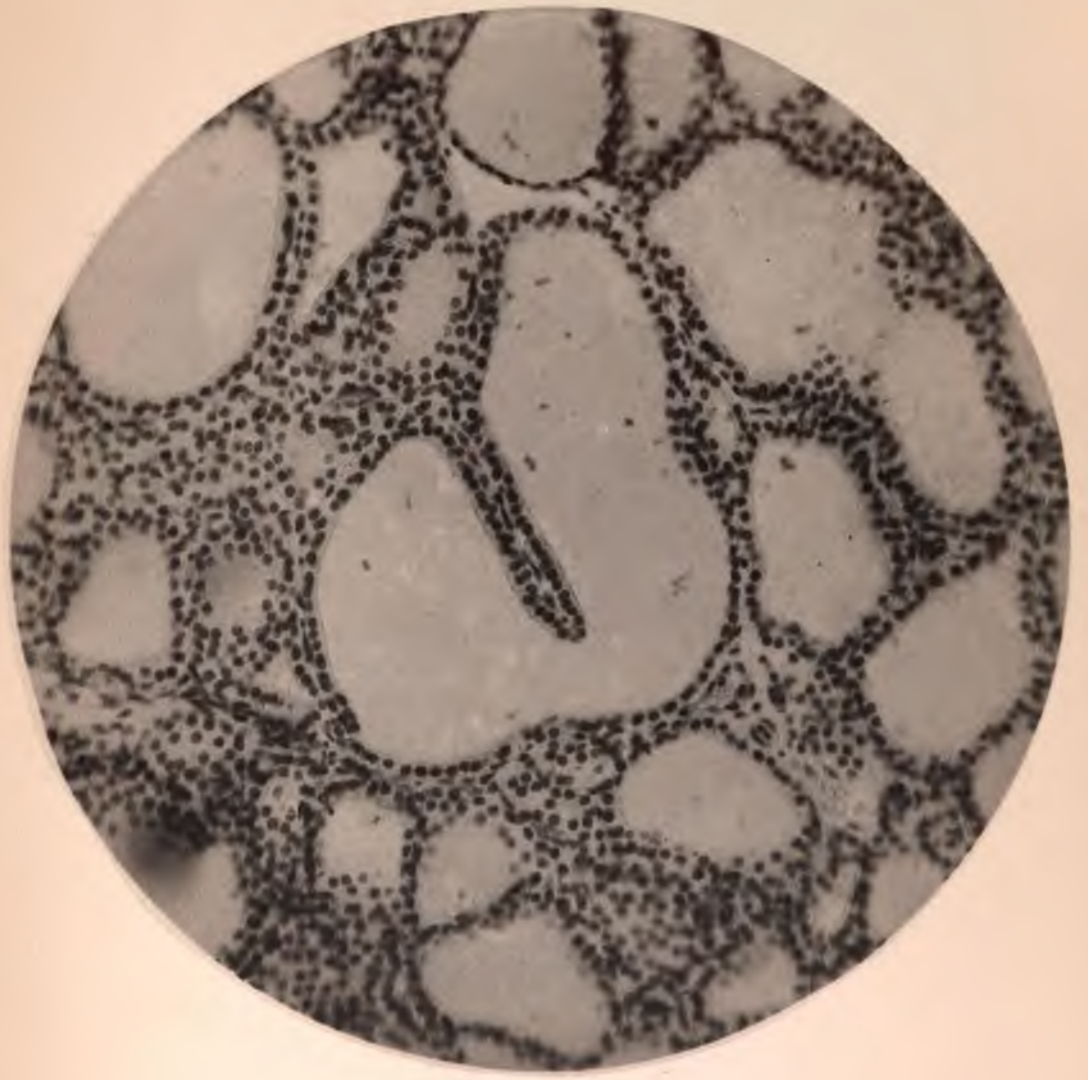




PHOTOGRAPH V.

275 diameters.

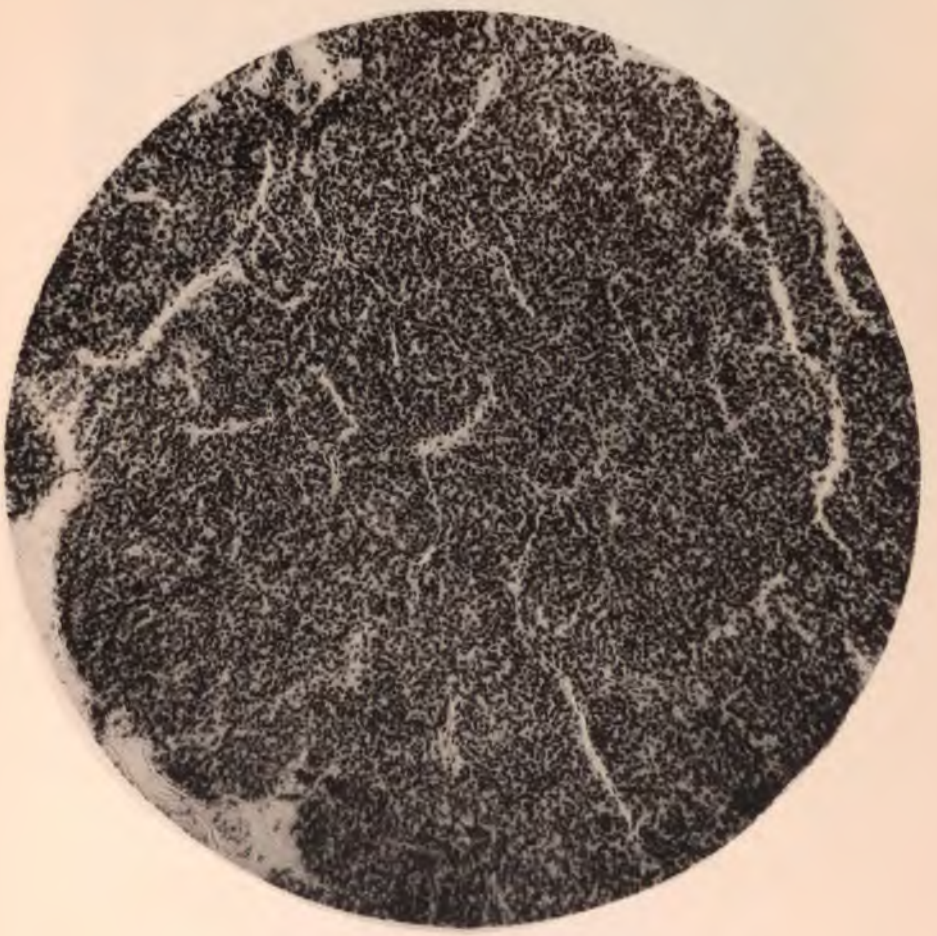
THE HELIOTYPE PRINTING CO., BOSTON



PHOTOGRAPH VI.

275 diameters.

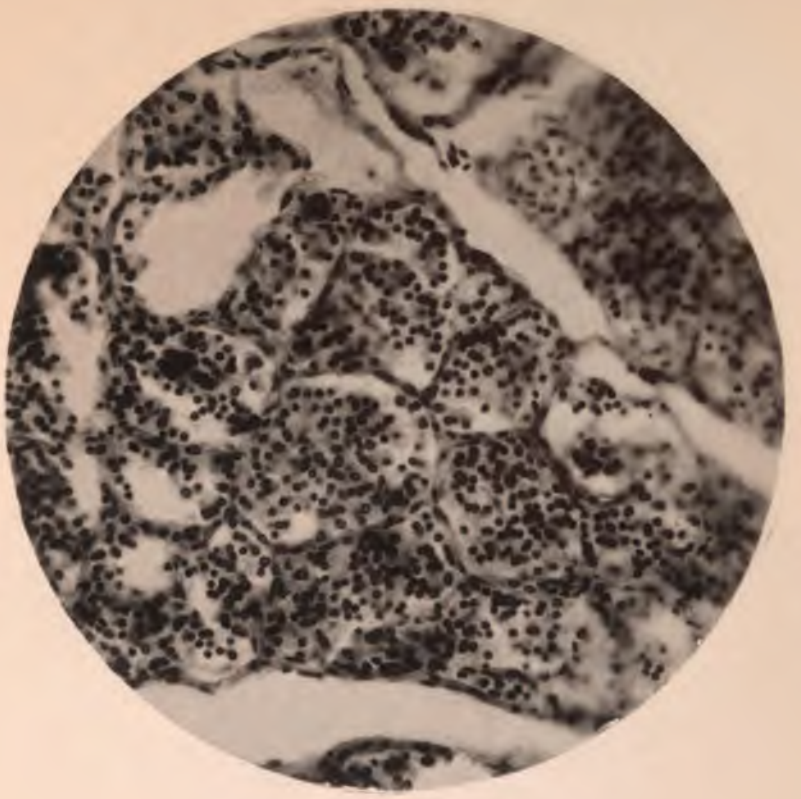
THE HELIOTYPE PRINTING CO., BOSTON



PHOTOGRAPH VII.

68 diameters.

THE HELIOTYPE PRINTING CO., BOSTON.



PHOTOGRAPH VIII.
275 diameters.

PHOTOGRAPH IX.
12 diameters.

THE HELIOTYPE PRINTING CO., BOSTON

PHOTOGRAPH X.

12 diameters.

THE HELIOTYPE PRINTING CO., BOSTON

Fig. 1.

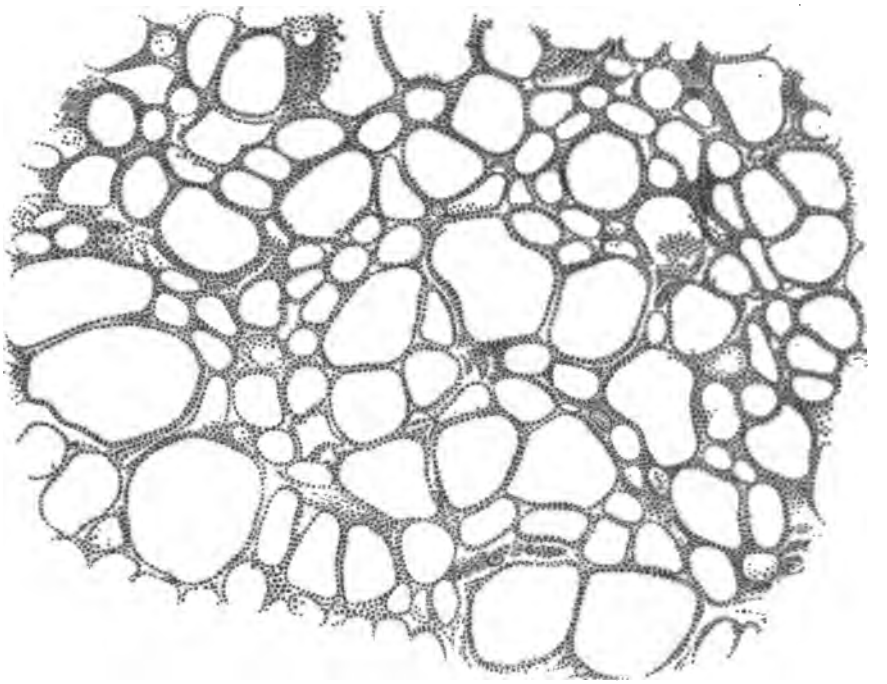


Fig. 2.

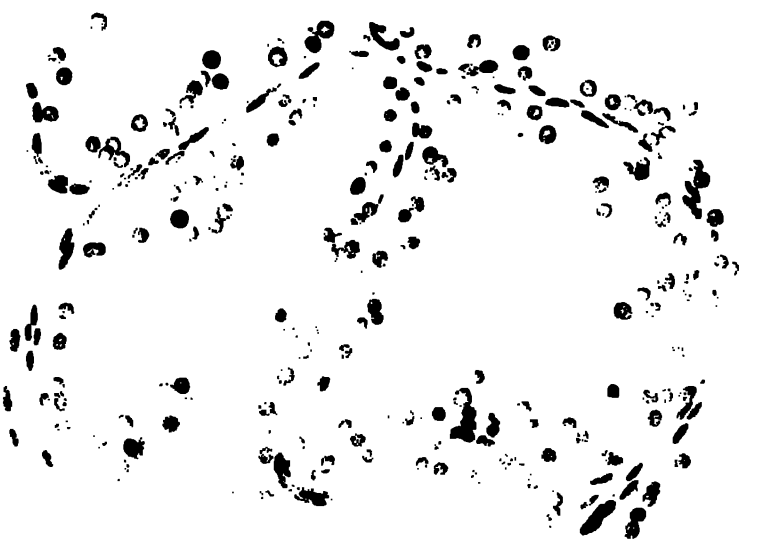
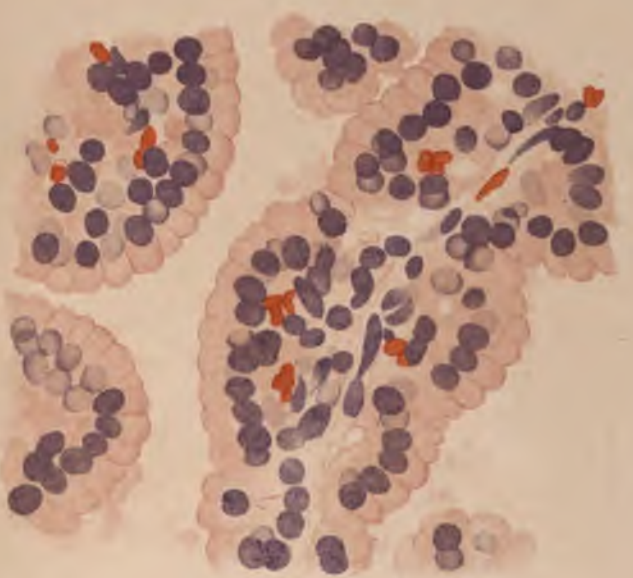


Fig. 3.

Fig. 4.



Lith. Anstalt v. J. Pecile, Lugano.

Fig. 5.

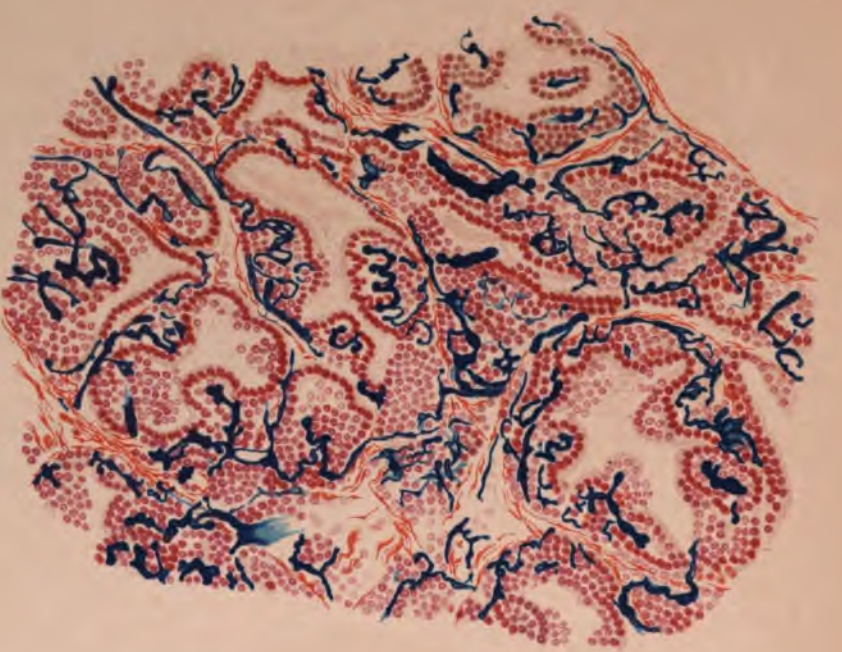


Fig. 6

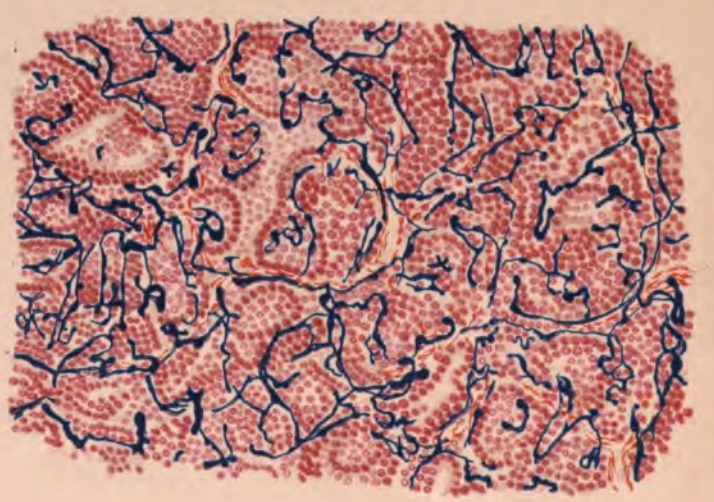


Fig. 7.

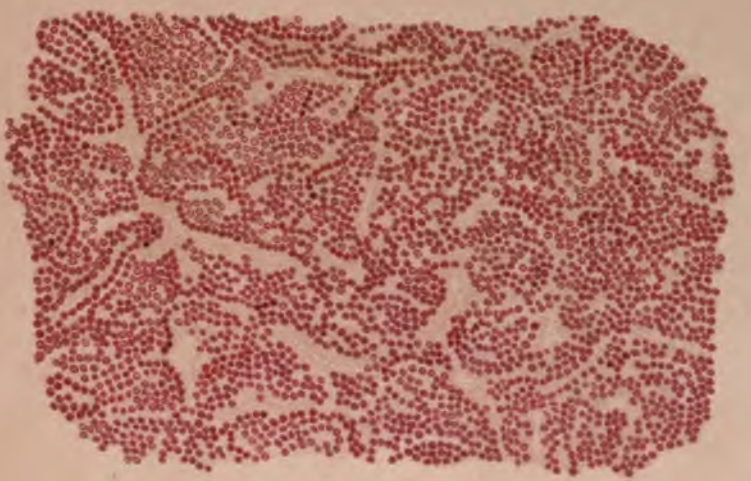
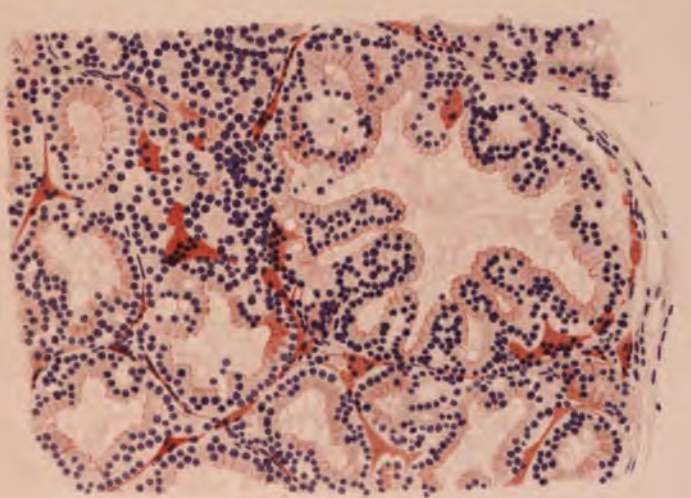


Fig. 9.

Fig. 8.




Makers
PAT. JAN. 21, 1908
L655 Halsted,W.S. 13347
H19 Experimental study of
1896 the thyroid gland of
NAME dogs.
DATE DUE